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THE MEDICAL CLINICS
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VOLUME 1 NUMBER 3

CLINIC OF DR. WARFIELD T. LONGCOPE

PRESBYTERIAN HOSPITAL

ACUTE TUBERCULOSIS; POLYCYTHEMIA WITH ENLARGED SPLEEN (VAQUEZ'S DISEASE). PRESENTATION OF CASES BY CLINICAL CLERKS. DISCUSSION OF CASES BY DR. LONGCOPE

CASE I

THE first patient is twenty-nine years old, a brass-foundry worker by trade, who was born in Ireland, but has been in this country for the past six years. His chief complaint on admission to the hospital was pain in the left chest, chilliness, cough, weakness, and loss of appetite, which had persisted for three days. The onset was sudden, with chilly sensations and fever, following two or three days' cold, cough, and night-sweating. The family history is negative except for the fact that his paternal grandfather (who lived next door to him) died twelve years ago of some lung trouble which was preceded by a severe cold.

Personal History.—The patient works in a brass foundry at heavy physical labor nine hours a day; he is in drafts most of the time and sweats profusely. He lives on the ground floor and has very poor light and air in his rooms. His appetite is never good; his bowels have always been regular until two or three months ago, since which time he has been constipated and has had occasional attacks of indigestion. His micturition has been normal. He takes two cups of tea a day; no tobacco or coffee;

an occasional whisky and 6 or 7 glasses of beer a day. Every three or four months he drinks to intoxication, but this lasts only a day or so. Occasionally he has severe headaches.

Past History.—The patient had measles as child, with good recovery, and an attack of pleurisy, about which he remembers very little. Since childhood he has been well and does not remember any illnesses. He had an infection some time ago, for which he visited the dispensary and was treated by wet dressing; later he had a sore throat. Venereal disease is denied. One year ago he fell down and struck his chest and immediately afterward brought up blood. He has never noticed any blood in the sputum since. His best weight is 140 pounds; he does not think he has lost any weight. For the past two or three months he has had cough and colds, with little sputum, occasionally he has sweated profusely at night; for a week or two before the onset of the present illness he had loss of appetite and felt weak and poorly. There was no history of any exposure except to drafts during his work, which he thought might have been a possible cause of this illness.

Present Illness.—Three days before admission the patient experienced chilly sensations and fever. He stayed at home on that day, and two days before admission he felt nauseated, tried to vomit, and did so after drinking warm water. The following day he experienced cramp-like pains in the lower left chest, which became sharper, and later were localized to the left axilla or posteriorly over the left shoulder. The pain was very sharp and was made worse by breathing. He had no appetite, his bowels were constipated, and he felt weak and occasionally dizzy.

The *physical examination* on admission to the hospital showed a man who looked very sick, had an increased respiratory rate, fever, no cyanosis and not much pain, but who was quite weak and prostrated, and was perspiring very profusely. The pupils were slightly dilated, the left a little larger than the right, they reacted promptly to light, but never contracted below mid-dilatation. His tongue was coated, teeth very bad, breath foul, and throat moderately reddened. There was a systolic pulsation in the neck; the thyroid was slightly enlarged. The

superficial lymph-nodes were shotty, but not markedly enlarged, though they could be felt in the cervical, axillary, and inguinal regions.

The chest expansion was good. Over the lungs there was slight dulness at the left apex and the inspiratory sound had a slightly bronchial character; there were coarse and fine moist râles over the left upper lobe and a few were heard over the right upper lobe.

The remainder of the physical examination showed nothing abnormal. The urine showed a specific gravity of 1027; it was clear, acid, there was a faint trace of albumin, no sugar, and microscopically an occasional granular cast and leukocyte. The leukocyte count was 16,500, with 79 per cent. of polymorphonuclears. There was very little sputum, which was thick and greenish in color. The temperature at the time of admission was 102.5° F., but rose shortly after admission to 104° F., dropping the next morning, and then rising to 105.5° F. Since then the temperature has gradually fallen by lysis to normal on the tenth day of the disease. The pulse-rate was rapid (120) on admission, and fluctuated with the curve of temperature. The pulse, too, is now normal in rate or even a little slow, for this morning it is 65. The respirations on admission were comparatively rapid (32), and for the first two or three days they were constantly above 30; gradually, however, they have diminished in rate, until this morning they are 24. The temperature, pulse-rate, and respirations have slowly come to normal on the tenth day of the disease.

Dr. Longcope: Have the physical signs changed during this time?

Clinical Clerk: Shortly after admission, when the fever was at its height, there were signs of complete solidification of the left upper lobe and possibly the upper part of the left lower lobe. Since then these signs have cleared somewhat, so that there are now signs of partial solidification in these regions with many râles at the left apex. At the present time an examination of the lungs shows the following signs: Over the left chest anteriorly there is diminished excursion, with increased tactile fremitus to

the fourth rib. Over this region the percussion-note is dull, above the left clavicle there is tubular breathing, below the clavicle the respiratory sounds are bronchovesicular in quality, and there are great numbers of coarse moist râles. In the third and fourth interspaces there is suppression of breath sounds. Beneath the clavicle there is bronchophony and the whispered sounds are high pitched and clearly heard. Posteriorly on the left there is dulness to the midinterscapular region, with increased tactile fremitus, bronchovesicular respiration, many coarse râles, bronchophony, and moderately high-pitched whispered sounds over this area.

The heart impulse is slightly forceful but regular, and there are no adventitious sounds. The remainder of the physical examination shows nothing abnormal.

Dr. Longcope: The patient, therefore, has been admitted to the hospital with an illness of acute onset accompanied by chills and fever and characterized by signs of solidification of the left lung that have persisted after defervescence of fever and subsidence of symptoms. Together with these signs there is a peristent leukocytosis, for yesterday the leukocytes were 17,000, with 83 per cent. polymorphonuclears.

This infection, for such it must be, has manifested itself, first, by general symptoms, and, second, by the local process in the lung, the signs of which we can so readily elicit. Gradually the symptoms and signs of the general intoxication or infection, or both, have almost entirely subsided, but the local disease of the lung persists. Without further study one might readily have suspected that this patient had suffered from an attack of acute lobar pneumonia with solidification of the left upper lobe which at the present time is slowly resolving. But from the moment the patient entered the hospital every effort was made to discover the exact etiology of his infection. Blood-cultures gave no growth of bacteria. The urine showed no precipitate with antipneumococcus serum of types I, II, or III. Cultures of the sputum and inoculations into mice did not show pneumococcus, but hemolytic streptococcus. Examination of the smears showed tubercle bacilli which are quite numerous; very easily

found and found on three separate occasions. How, therefore, do you characterize this case?

CLINICAL CLERK: The possibilities are that the patient has had chronic pulmonary tuberculosis with an acute lobar pneumonia engrafted upon it, or that he has had an acute tuberculous pneumonia. When the patient first was admitted to the hospital he was supposed to have lobar pneumonia. If the sputum had not been examined for tubercle bacilli the diagnosis of acute lobar pneumonia with beginning resolution of a consolidation of the left upper lobe and recovery by lysis would have been made.

DR. LONGCOPE: Is it possible to exclude the fact that this patient has had lobar pneumonia, or is there any evidence that he has had lobar pneumonia?

CLINICAL CLERK: We have no bacteriologic evidence of an infection by pneumococcus. It might be that the acute symptoms were caused by an infection with hemolytic streptococci.

DR. LONGCOPE: Has the hemolytic streptococcus been constantly present?

CLINICAL CLERK: The preliminary examination showed this organism, but since then there have been no cultures of the sputum.

DR. LONGCOPE: At one time it was thought that cases of lobar pneumonia which were due to the pneumococcus predisposed to or terminated in tuberculosis of the lung. Without further examination one might be tempted to assume that this patient was suffering from pneumonia caused by Streptococcus hæmolyticus. Smears of the sputum as well as cultures were examined.

It is well known, however, that such a series of events exist almost exclusively in the conceit of the physician and not in the workings of nature, and that tuberculous pneumonia is tuberculous from the start and not secondary to a pneumonia caused by some other organism. It is, of course, possible for a tuberculous patient to have an acute lobar pneumonia caused by the pneumococcus, but in the vast majority of cases signs of lobar pneumonia and symptoms of acute infection in cases of chronic

tuberculosis are caused by an acute tuberculous process involving the lungs.

The cause of the sudden and acute involvement of the pulmonary tissue in these cases of tuberculous pneumonia is one of great interest and importance. It may come about by spread of tubercle bacilli from an old latent focus in the lung itself or from a fresh infection from without. The commonest method is from a chronic focus of infection in the lung itself. This theory is held to very strongly by Röhmer, who believes that all acute tuberculosis in adults originates from a chronic infection attained originally in early youth or childhood, for the adult is much more resistant to tuberculosis than the child, who after infection may attain a certain degree of resistance. The other possibility is that the disease is communicated by direct infection from one individual to another, and that the onset of a rapidly progressive acute process in adult life is the primary infection. There is evidence in this man to show that he has had symptoms if not signs of a tuberculous lesion in his lung. The assumption, therefore, is that an acute process has developed from a chronic lesion some time before the onset of the acute pneumonic process.

Whether the acute pneumonic process arises from a chronic latent lesion in the lung or in some other portion of the body, or whether in a tuberculous subject it is incited by inhalation of tubercle bacilli from without, there is evidence to show that the spread or re-infection in a tuberculous patient runs a different course from the primary infection in a healthy individual. In the latter instance the local spread of infection is rapid, the reaction violent, but fortunately in such cases, as in the present instance, it may subside comparatively soon.

x-Rays of the chest (Fig. 44) show not only involvement of the left lung, but of the right lung as well. The upper portion of the left lung is most extensively involved, as you see by the plates. The right lung at the root and upper portion of the lobe is likewise involved. The shadow in this plate is somewhat different from the shadow one sees in most cases of lobar pneumonia, where there is a diffuse, evenly distributed shadow over the consolidated lung; for here the consolidation is in small irregular

spots, as if there was coarse stippling all over the upper portion of the left lung and with involvement on the right side as well.

In the lung the pathologic process may assume: first, the

Fig. 44.—Case I.

rapidly spreading type of caseous pneumonia; second, the gelatinous pneumonia, in which the exudate is formed of large numbers of epithelioid cells filled with lipoids; third, the acute tuberculous

peribronchitis, which goes on rapidly to a bronchopneumonia with destruction of bronchi and multiple cavity formation. It is very probable that this man has one of these types of pathologic lesion.

Demonstration of Lantern Slides.—The first illustration shows you the characteristic gross appearance of the caseous pneumonia. You may see that almost the entire upper lobe of the lung is converted into a solid opaque cheesy material.

The second illustration represents a fair example of acute gelatinous pneumonia. Here there are small patches of caseation scattered through the lung and surrounded and separated by large gray translucent areas which involve almost the entire lobe. This drawing of a microscopic section from one of the gelatinous areas shows that the alveoli are packed with large epithelioid cells which are often filled with fat and lipoid droplets. There are practically no polymorphonuclear leukocytes in these sections and they do not form a conspicuous element in the exudates in this pathologic process.

The last picture represents the gross appearance in a case of peribronchial tuberculous bronchopneumonia, where large areas of solidification surround the bronchi, that are in places dilated and in others lead directly into small cavities.

In cases of caseous and gelatinous pneumonia there may be little sputum, and it is often with great difficulty that one discovers tubercle bacilli in the sputum that is obtained. This fact is readily understood, for until the solid caseous material softens there is little exudate into the bronchi and, therefore, no sputum. This man whom we have just seen has had considerable quantities of sputum in which there were large numbers of tubercle bacilli, and it is possible for this reason that this patient is representative of the type of case who suffers from a peribronchial tuberculosis rather than from a caseous or extensive gelatinous pneumonia.

CASE II

Presentation by Clinical Clerk.—The second case is a Bohemian, about fifty-three years old, who speaks no English and no German. The history was obtained from his wife, who

speaks a very limited amount of English, so that the history is deficient. He has worked as a type-setter all his life. This is all we can learn about his habits. His diet is regular; he takes three cups of coffee and two of tea a day, and formerly, up to ten years ago, drank a good deal of alcohol, often coming home intoxicated. His wife says that he has always had a very red countenance. When four years old he fell, according to his wife, and the left leg has always been weaker and shorter than the right since that time. His chief complaint is stiffness in the right arm, which came on about two months ago, together with an indefinite illness of about a year's duration. He has had fulness in the head, headache, and at times dizziness, which is quite marked every now and then, and ringing in the ears. There has been no weakness and no pain in any of the muscles. He has been constipated all his life. Urination is not quite normal, for he voids three or four times during the day and twice at night. His wife says he has taken no medicines.

Present Illness.—Stiffness in the right hand started about two months ago, apparently in the fingers, and became progressive, involving the whole arm. The leg was later affected. His wife has also noticed that his speech has become heavy and more guttural in type, but he can speak Bohemian to his wife without very much trouble. He has not done any work for the last two months. He cannot rise now without assistance. He has never had nosebleeds nor bleeding from any of the mucous surfaces, none from the kidney, and none in the stools.

Physical Examination.—The neurologic examination is limited because the patient cannot assist. An examination of the eyes shows the following: ophthalmoscopic examination shows that both fundi are pinkish, vessels quite markedly prominent, but are not tortuous; the disks are clear; there are no hemorrhages. Eye movements are normal; no ptosis, no nystagmus, no limitation of movement. How much he could see one could not tell. The movements of both sides of the face are symmetric. When he shows his teeth and at times when he talks the right side is pulled over to the left and an absence of creases is noticeable on the left side.

When he tries to show his teeth the left side of the face is drawn well over and down. The nasolabial fold on the right side is not nearly so well marked as on the left and the corner of the mouth does not move so much. There is evidence of weakness of the lower right facial muscles. The tongue protrudes straight. The reflexes are present on both sides. There is elevation of the right shoulder, which also seems to be closer to the median line, and the scapular muscles are diminished, as well as those of the upper arm. In the left arm the reflexes are active and all present, including pectoral, biceps, triceps, and radial. In the right arm the reflexes are more active. There seems to be a definite contraction of the biceps. The intercostal muscles and thorax in general on the right side is drawn over to the left on deep inspiration, as if on a pivot. In the abdomen there is stiffness of the right side to a very slight extent. The abdominal reflexes are absent on the right side. An examination of the right leg does not show the stiffness which is present in the upper extremity. The Achilles jerk cannot be obtained on the left, but is present on the right and active, while the knee-jerk is very active on the right side. No ankle-clonus is obtained and there is no Babinski. There does not seem to be any tenderness anywhere. Lower periosteal reflex is present on the right, but there is no cross periosteal.

These findings indicate that the hemiplegia is due to a lesion in the upper motor neurons involving the tracts for the lower portion of the face, to a slight extent the thorax, abdomen, and the leg. The condition has lasted for some time, and has resulted in secondary changes which result in spasticity of the muscles of the arm with increased tendon reflexes on the right side.

Dr. Longcope: This is the trouble which disturbs him most, but it is only a symptom or complication of the disease from which he is actually suffering.

The most striking thing about this man is his color. He is noticeably florid. The ears are deep purplish-red in color or reddish-purple. The nose is not so deeply colored as it was the other day when I saw him, but even now the nose, lips, and

conjunctivæ are red, the latter covered with dilated veins. The tongue is an extraordinary deep magenta. The hands, even when he holds them up, are quite purplish-blue in color. This tint is also very marked about the neck. The feet the other day were of the same curious purplish red. Everywhere the skin is dark reddish in color, but this is most marked about the face, neck, ears, hands, and feet.

Now this is associated with certain other findings that are most interesting. First, the dilatation of the blood-vessels; both the small blood-vessels of the skin and the large veins over the extremities. See the veins over the feet, they look like heavy blue cords. Notice those also over the tibiæ and over the legs. The veins in the conjunctivæ are enlarged and the veins in the fundus of the eye are very large and tortuous. The smaller veins over the forehead show some dilatation as well as those over his arms, which are larger on the right arm than on the left. Besides these tortuous veins there are groups of minute dilated veins and reddish-purple spots which are seen scattered over the chest, the upper portion of the abdomen, and over the right arm particularly.

Second, observe the clubbing of the fingers. The fingers of the right hand show this particularly well and the clubbing of the thumb is very marked. In contrast to the right hand the left shows no definite clubbing of the fingers. There is, I think, some suggestion of clubbing of the toes, which are very broad. Again, this is more marked on the right side than on the left. The nails are a little bit curved, the pads of the toes are thick, but this is not so marked as it is in the fingers.

The remainder of the physical examination discloses the following findings: In the chest there is slight dulness posteriorly at the bases of the lungs and a few coarse râles are heard in this region during inspiration.

The heart is slightly enlarged. The maximum impulse lies in the fifth space just outside the nipple. The cardiac dulness reaches 12.5 cm. to the left in the fifth space. At the apex the first sound is prolonged and booming; the second sound is short. At the base the heart sounds are even more distinct, and at the

aortic area the second sound is accentuated. The systolic pressure is 140, the diastolic 85. The abdomen is somewhat protuberant. A large hard mass is readily palpable in the left hypochondrium, which has a rounded edge, descends on respiration, and assumes the shape and position of a greatly enlarged spleen. It is not tender. The liver and kidneys are not palpable.

The examination of this man's urine shows the following:

4/19: 1023, acid, flocculent, alb. tr., gluc. 0, few urates, few W. B. C.
4/20: 1022, acid, flocculent, alb. tr., gluc. 0, few urates, few W. B. C., few hyal. casts.
5/11: 1011, alb. tr., gluc. 0, few urates, few W. B. C.

Finally, an examination of the blood, which is of utmost importance, completes the clinical picture of the disease from which this patient is suffering. The blood examination on admission, April 18, 1917, was as follows:

R. B. C. 8,000,000. Hgb. 120 per cent. (Hassler). W. B. C. 18,100.
Polys.: Neutro. 80 per cent. Lymphos. 17 per cent.
Eosin. 1. Large mon. 2. Smear normal. 100 cells.

The hemoglobin is 130 per cent., the red cell count on various occasions has been: 8,000,000, 8,400,000, 7,900,000, and the leukocytes: 12,000, with 82 per cent. polymorphonuclear leukocytes.

The diagnosis is, Vaquez's disease: polycythemia with cyanosis and enlarged spleen.

This is a striking example of this rather unusual and very obscure disease, presenting certain features of especial interest; namely, the clubbing of the fingers and toes and the complicating hemiplegia.

The clinical picture was first recognized and accurately described by Vaquez in 1892, though it was not until Osler described vividly a series of cases in 1903 in the American Journal of Medical Sciences that the disease became familiar to the medical public and was recognized generally as a clinical entity. Since then Senator, in his monograph on "Polycythæmia und Plethora," has considered the entire subject from a broad standpoint, while Lucas has reported carefully a series of 79 cases collected

from the literature. From the original clinical entity Giesbock has separated a special group which he has termed polycythemia hypertonica, a condition which is characterized by polycythemia, cyanosis, and hypertension without splenic enlargement.

The case before you is evidently not of this latter type, but belongs to the group originally described by Vaquez.

The symptoms in these cases may be referred to the skin itself, the purplish cyanosis being the predominant feature; rarely to the mass in the abdomen, the enlarged spleen; occasionally to nosebleeds, for hemorrhage from the mucous surfaces and, indeed, occasionally from large vessels is not uncommon; or perhaps most common of all, to symptoms referable to the nervous system, tinnitus, headaches, and attacks of vertigo. Peripheral venous thrombosis has been recorded as a complication in many cases, and during the last three years I have seen 2 cases of Vaquez's disease who died with this complication. Hemiplegia has occasionally been noted as a complication and may, indeed, be a result of thrombosis of the cerebral vessels. It is not improbable that the partial hemiplegia in the case which has just been presented to you is the result of thrombosis of one of the smaller cerebral vessels. The clubbed fingers which are such an interesting feature of the present case have rarely been observed before in this disease.

A study of the morbid anatomy of the fatal cases has shown quite regularly a marked hyperplasia of the bone-marrow which appears deep purple in color, an enlarged spleen which in a few cases has been the seat of tuberculosis, but no other characteristic changes that throw any light upon the nature of the disease.

Interesting information has been obtained from investigations upon the anatomy and physiology of the blood during life, and all evidence goes to show that there is an actual increased production of red cells. It has been shown that there is a total increase in the amount of blood, with increased viscosity, and a specific gravity which is usually normal. In this instance the specific gravity of the blood was 1086, but, as a rule, it has been recorded as averaging between 1054 and 1056. The percentage of cells to plasma is greatly increased. In this instance it was almost

impossible to separate the cells from the plasma after ten minutes' centrifugation. From 10 c.c. of blood, however, 3 c.c. of plasma were obtained.

In morphology, the red cells appear, as a rule, normal in size and shape, though occasionally nucleated red blood-cells are seen. In this particular instance they have not been found. The total number of white cells is increased to 30,000 or 40,000, but in this case they are approximately normal. The platelets are not changed and in this patient were normal in number, being 300,000. The coagulation and bleeding time are both short. The coagulation time was three minutes and the bleeding time one minute in this patient.

Much study has been devoted to determine the origin of this peculiar condition and to explain the exciting cause for the polycythemia.

It has been supposed by some that the condition had its origin as a primary disease of the spleen, and I have already mentioned that tuberculosis of the spleen has been found in a few instances. Cases have, however, come to autopsy which have not had tuberculosis of the spleen, and it does not seem probable that any gross lesion such as tuberculosis or syphilis of the spleen can account for the entire course of the disease. The Wassermann reaction in this patient is negative. That the spleen is in some way involved in this symptom complex is obvious, but whether the enlargement is primary or secondary and represents an accompanying condition cannot at the present time be determined.

Many of the causes of polycythemia which are more or less clearly understood do not exist in these cases of Vaquez's disease. Since the increase in red cells is absolute and not relative, any explanation which would depend solely upon a disproportion between the total cell volume and plasma volume, such as occurs in severe diarrheas when large quantities of fluid are lost to the body, is naturally untenable.

There is no evidence to thow either that the polycythemia is in any way analogous to that produced by adrenalin, under which circumstances it now seems probable from the work of Lampson that erythrocytes stored especially in the liver are suddenly

expelled into the circulation. Nor is there any evidence to show that the polycythemia is in any way dependent upon a lack of oxygen-carrying capacity of the red cells. It is well known that chronic carbon monoxid poisoning in animals results in a polycythemia and increased production of red cells. This depends upon the constant conversion of a certain proportion of hemoglobin into carbon monoxid hemoglobin, thus impoverishing the oxygen-carrying capacity of the blood and necessitating an excessive production of red blood-cells to compensate for the "dead wood." The theory that this disease is dependent upon the formation of some chemically stable hemoglobin compound, which renders that substance partially unavailable for the formation of oxyhemoglobin is untenable, since Butterfield has found the oxygen-carrying capacity of the blood normal in Vaquez's disease.

The possibility that a constantly increased destruction of red cells by autohemolysins or chemical substances might excite an increased production of erythrocytes has been brought forward as a suggestion to explain the polycythemia, but no evidence has yet been adduced to uphold this idea.

That the difficulty lies rather in a diminished destruction of red cells with a normal production has also been taken into consideration, but all evidence goes to show that the actual state of affairs is exactly the reverse.

You may see, then, how obscure is the etiology and pathologic physiology of this interesting disease, and under these circumstances I need hardly emphasize the fact that all therapeutic measures which have been tried in these cases have proved more or less unsatisfactory.

The spleen has been *x*-rayed and, in a few instances, removed. Radium has been applied to the spleen and long bones, but without noticeably good effect. The only effective therapeutic measure seems to be repeated bleeding which may relieve such symptoms as headaches, tinnitus aurium, and vertigo, but affords neither permanent relief from symptoms nor a deterrant effect upon the course of the disease. Fortunately the disease is chronic, and these patients may live for many years suffering but slight discomfort.

CONTRIBUTION BY PROF. GRAHAM LUSK

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CALORIES IN COMMON LIFE

An Estimate of Food Requirements in Health and Disease

A PERSON is properly nourished who receives adequate energy in the form of carbohydrate and fat (and incidentally protein); adequate material for repair of wornout parts, such as protein and mineral salts; and the diet must contain certain accessory food substances known as food hormones or "vitamins." Also, it must contain water. But this is not all, for the food offered must be acceptable to the palate of the individual. A member of the French Scientific Commission which visited the United States in the summer of 1917, when questioned regarding the use of corn bread in France, replied "on ne peut pas changer des habitudes." The proper nutrition of an individual depends, therefore, not only upon a sufficient supply of food from a mechanistic standpoint, but also upon the reasonable satisfaction of the sense of appetite. These dual fundamentals of proper nutrition should be ever borne in mind.

Science strives to express itself in mathematic terms, and this paper is written with that end in view.

Phenomena of life are phenomena of motion. These motions are maintained at the expense of chemical energy liberated in the oxidative breakdown of carbohydrate, fat, and protein. Furthermore, the protein structure of the body cells and the salts of the bones and other tissues is in a constant state of wearing down. The energy for the human machine and the materials

for its self-repair are taken in the form of food. The general term *metabolism* includes all the chemical activities which take place under the influence of living cells.

The total quantity of heat produced by the body is a measure of the intensity of the oxidation of carbohydrate, fat, and protein within the body.

When a man lies quietly at rest upon a comfortable bed in the morning before partaking of breakfast his metabolism is at the lowest level. He requires energy (1) to maintain the heart-beat; (2) to maintain the muscles of respiration; (3) to maintain the manifold activities of the cellular life within his body; and (4) to mainain the body temperature at a constant level. When one measures the heat production under these circumstances one obtains what is called the *basal metabolism.* Any extraneous work, such as lifting the arm or rolling over in bed, is accomplished only at the expense of additional heat production. In certain pathologic conditions the basal metabolism may be increased and in others decreased. It is important to know definitely whether there is any constant measure of the level of the basal metabolism in normal people, so that one may determine in cases of disease whether the heat production is normal or increased or decreased.

Rubner discovered that the heat production of mammalia during rest was the same per square meter of surface whether the being was a horse, a man, a dog, or a mouse. The proposition has appeared so improbable as to call forth much antagonism. DuBois deserves the credit of having established this relationship for man beyond the possibility of a doubt. He was able to do this on account of his discovery of a new and accurate method of measuring the area of the body surface. It appears from his work that the *basal metabolism* for men between twenty and fifty years old is approximately 40 calories per hour per square meter of body surface, within a $\pm$ error of 10 per cent.

Boothby has found that the metabolism of patients who have recovered their health after hospital operations and who have been confined in the hospital between twenty and fifty days conform to the normal standard of DuBois.

It has been found by DuBois that the basal metabolism in boys of twelve, just prior to the onset of puberty, is 25 per cent. higher than for an adult of the same height and weight, or 50 calories per square meter of body surface; and that in boys of fifteen, after puberty, the metabolism is 11 per cent. higher than for the adult of the same size and shape, or 44 calories per square meter of body surface (unpublished work of DuBois). These results explain the large appetites of boys.

Women show a metabolism which is 7 per cent. lower than that of men, or 37 calories per hour per square meter of surface. This is independent of the menstrual period or of the period of pregnancy.

From the charts of the average heights and weights of men varying between fifteen and fifty-five years old, given by American life insurance companies, Mr. H. V. Atkinson, of my laboratory, has calculated the basal metabolism in a table here presented (p. 484). The table is based on the following values:

Age in years.	Calories per square meter of surface.
15	44
20–50	40
55	37

The table may also be used as follows:

To find the metabolism of—

Women between twenty to fifty years, multiply values for man by 0.93.

Boys of twelve to thirteen years, multiply values for boys of fifteen years by 1.10.

THE BASAL METABOLISM OF MEN

Calculated from values of the basal metabolism determined by the methods of DuBois and applied to a table showing the average weights of 221,819 men of different ages and heights compiled from the statistics of the medico-actuarial investigation of 1912.

Age. Heat per square meter of surface.	5 ft. 0 in.	5 ft. 2 in.	5 ft. 4 in.	5 ft. 6 in.	5 ft. 8 in.	6 ft. 10 in.	6 ft. 0 in.	6 ft. 2 in.	6 ft. 4 in.
	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.	Lbs. Cals.
15 years	107	112	118	126	134	142	152	162	172
44 calories	1510	1584	1658	1753	1837	1922	2006	2096	2186
20 years	117	122	128	136	144	152	161	171	181
40 calories	1430	1498	1565	1647	1719	1796	1868	1949	2035
25 years	122	126	133	141	149	157	167	179	189
40 calories	1459	1517	1594	1671	1738	1820	1896	1992	2083
30 years	126	130	136	144	152	161	172	184	196
40 calories	1478	1536	1604	1685	1757	1839	1920	2007	2112
35 years	128	132	138	146	155	165	176	189	201
40 calories	1488	1556	1613	1695	1767	1853	1939	2035	2136
40 years	131	135	141	149	158	168	180	193	206
40 calories	1498	1565	1623	1709	1781	1863	1959	2055	2160
45 years	133	137	143	151	160	170	182	195	209
40 calories	1507	1570	1632	1719	1791	1872	1968	2064	2169
50 years	134	138	144	152	161	171	183	197	211
40 calories	1517	1575	1642	1724	1796	1881	1973	2074	2184
55 years	135	139	145	153	163	173	184	198	212
37 calories	1449	1485	1548	1620	1692	1773	1854	1949	2052

The basal metabolism of an average boy of thirteen years of age weighing 80 pounds and of a height of 4 feet, 10 inches, may be calculated as 1525 calories per day. This is the same as that of a man twenty-five years old, weighing 126 pounds and 5 feet, 2 inches tall.

A boy thirteen years old and weighing 156 pounds, his height being 6 feet, 1 inch (there are such cases), would have a basal metabolism of 2300 calories, or larger than that of any grown man given in the table, larger than a man weighing 211 pounds and 6 feet, 4 inches in height.

It is evident from this discussion that the food requirement of boys over twelve years old is about the same as that of men.

The emaciation of the children of the poor probably reduces their requirement of food. It is not generally recognized that the boy needs as much food as the father. The requirements of girls have not been investigated, but they probably need as much as their mothers.

These data will give with close scientific precision the *minimal requirement for energy* which is necessary for the maintenance of the bed-ridden.

Ordinary life, however, is not constituted after this fashion. "By the sweat of thy brow shalt thou eat bread."

From the work of F. G. Benedict one may calculate the increase in the basal metabolism, as follows:

Occupation.	Increase in the basal metabolism in per cent.
Sitting	5
Standing, relaxed	10
Standing, hand on a staff	11
Standing, leaning on support	3
Standing, "attention"	14

If one wishes to determine the heat production of a person who is confined to his room from the basal metabolism table, one should add to the metabolism of the twenty-four hours the increase above the basal for those hours of the day during which he is sitting in a chair or standing.

Passing to a consideration of the subject of mechanical work done by a man, one finds that it requires about 1.1 calory to transport a pound of body weight three miles during an hour, and that increasing power must be generated if the speed is increased above this rate of *maximal economic velocity*.

These relations are shown below:

Rate of movement.	Extra calories per hour required to move 1 pound of body.
Walking 3 miles per hour	1.1
Walking 5.3 miles per hour	3.6
Running 5.3 miles per hour	3.1

If one wishes to determine the heat production of a man weigh-

ing 156 pounds and 5 feet, 7 inches in height, and who is walking or running, the following calculations can be made:

Rate of travel per hour in miles.	3* Cals.	5.3* Cals.	5.3† Cals.
Metabolism for transporting 156 pounds	172	562	484
Basal metabolism	70	70	70
Add for standing	7	7	7
	249	639	561

* Walking. † Running.

If the man's food cost 10 cents a thousand calories, it may be calculated that he would have to walk over eight miles at a rate of three miles per hour in order to save money when he pays a 5-cent carfare. (This, however, does not include the cost of shoe leather.)

The carrying of a load of 44 pounds is done at the same expenditure of energy as the carrying of one's own body weight when the rate is three miles an hour, so the soldier's equipment would call for the added expenditure of 48 calories (44×1.1), making his total hourly expenditure of energy nearly 300 calories ($249 + 44$) during a hike on a level road. His daily requirement for energy might be:

	Calories.
Sleeping 8 hrs. at 70 cals. per hr.	560
Resting in camp 6 hrs. at 77 cals. per hr.	462
Hike of 30 miles, 10 hrs. at 300 cals. per hr.	3000
	4022

This assumes a level road. If, however, there are hills to climb and the body weight and the pack are lifted 1000 feet during the hike, this is done at the additional expense of approximately 0.96 calory of energy per pound of weight lifted. If the man weighed 156 pounds and the pack 44 pounds, the additional fuel requirement would be 192 calories (200×0.96). The total energy requirement for this kind of a hike would have been 4200 calories. Walking down hill is accomplished at an expenditure of slightly less energy than walking on the level, but this factor need not concern one.

Supposing, however, this individual were running, lightly clad, on a level road in a race for a distance of 40 miles at the rate of 5.3 miles per hour, he would complete the distance in seven hours and thirty-three minutes, which is a reasonable record. His metabolism might thus be calculated:

	Calories.
Sleeping 10 hrs. at 70 cals. per hr.	700
Resting 6 hrs., 23 min., at 77 cals. per hr.	497
Running 7 hrs., 33 min., at 561 cals. per hr.	4236
	5433

These calculations are all based upon experimental results obtained in various laboratories in different parts of the world and can be accepted as being free from any gross error.

It is evident that the energy requirement is proportional to the amount of mechanical energy expended.

One may turn now to the fuel needs in terms of calories in certain industrial pursuits. According to Becker and Hämäläinen, the quantity of extra metabolism per hour required in various pursuits is as follows:

	Extra calories of metabolism per hour due to occupation.
Occupations of women:	
Seamstress	6
Typist[1]	24
Seamstress using sewing machine	24– 57
Bookbinder	38– 63
Housemaid	81–157
Washerwoman	124–214
Occupations of men:	
Tailor	44
Bookbinder	81
Shoemaker	90
Carpenter	116–164
Metal worker	141
Painter (of furniture)	145
Stonemason	300
Man sawing wood	378

To use this table one may seek the basal metabolism of the

[1] Observation of Carpenter.

individual, add 10 per cent. for sixteen hours of wakefulness when the person is sitting or standing, and then multiply the factors in the last table by the numbers of hours of work. For example, if one takes the individual weighing 156 pounds, one obtains the following requirements of energy if his business were that of a tailor and he worked eight hours a day:

	Calories.
Sleeping 8 hrs. at 70 cals. per hr.	560
Awake 16 hrs. at 77 cals. per hr.	1232
Add for work as tailor 8 hrs. at 44 cals.	352
	2144

After this fashion one might calculate his food requirements had he followed occupations other than that of tailor, as follows:

Occupation.	Calories of metabolism per day.
Bookbinder	2440
Shoemaker	2510
Carpenter	3100
Metal worker	2900
Painter	2950
Stonemason	4200
Man sawing wood	4800

These figures make no allowance for walking to or from the place of employment.

The data here given are inadequate to cover the industrial situation, but they show clearly that heavy work cannot be accomplished without a sufficient amount of food-fuel.

The food-fuel with which to accomplish work is necessary not only for the soldier, but for the workman behind the line, and it should be adequate in quantity, satisfactory in quality, and not exhorbitant in cost.

In virtue of the worldwide scarcity of food, the work of the individual should be worthy of the food which he eats.

Milk contains all the fundamental food elements necessary for the welfare of mankind with the exception of the element of iron. It contains protein, fat, carbohydrate, water, salts, and the so-called "vitamins," of which two are believed to exist, the

one soluble in fat and the other in water (McCollum). The fundamental safeguard for the proper nutrition of the people is in the dairy farm. With an ample milk supply the health of a people is assured.

So far as is known, taking meat even in large excess in not harmful, but it represents luxury and waste. According to an oral statement by A. E. Taylor, the results of many thousand urinary analyses in Germany during the second year of the war showed about 7 grams of nitrogen excreted, which would correspond to a dietary containing about 45 grams of protein. As a matter of fact, this is the equivalent of the reduced protein dietary of Chittenden, and it is reported that no ill effects can be attributed to it. The flavor of meat is such that it lends itself to the easy preparation of a palatable meal, but this flavor could undoubtedly be as well obtained if the present consumption of meat were cut in two. It is a question of habit, but with the present reduced supply of meat one must adopt new habits. It would be highly desirable if the grain now fed to fatten beef were given to maintain herds of milch cows.

The intake of meat has no beneficial relation to the capacity for muscular work; in fact, an exclusive meat diet results in the sensation that work is being accomplished with difficulty. When meat is metabolized it stimulates the body to a higher heat production, as great an increase as 55 per cent. having been observed in a resting man. No other food-stuff will accomplish so great an increase. It is especially worthy of note that this increase in the heat production, due to the *specific dynamic action* of protein, as it is called, cannot be utilized in the execution of mechanical work. When the organism of a laborer at work in a hot environment is called upon to eliminate extra heat, due to the work he is performing, he must also eliminate the quota of heat which is derived from any large ingestion of meat. Hence, the American farmer in the hot weather can eat little meat.

The work of the world is accomplished mainly at the expense of the oxidation of carbohydrate within the organism. Under ordinary circumstances two-thirds of the total energy production is derived from glucose which is the product of the digestion of

starch. The bread, macaroni, and rice found in the dinner-pail of the laborer testify as to the source of his power. When such a laboring man works the glucose which enters his blood-stream is used for the production of that work, without itself increasing the heat production.

Cane-sugar is a valuable condiment as well as a food-stuff, and when taken in small quantities every half-hour may delay the onset of fatigue. It is more largely used in the United States than in other countries in the world. As a subsitute glucose may be used. This is found in grapes and in raisins, and it is also produced in large quantities by the hydrolysis of starch and sold under the commercial name of corn syrup or Karo. This substance is entirely wholesome and may be freely employed in the place of sugar, which is scarce.

Fat is a material which yields energy for the day's work in a manner similar to carbohydrate, which it may, under given conditions, supplant entirely or in part. Fats, however, are more expensive than carbohydrates. The animal fats are more expensive than those of vegetables. Cottonseed oil, for example, is much cheaper than butter or bacon and may be freely used. If whole milk is taken, 3 quarts a day for a family of five; butter which contains the fat soluble "vitamin" may be dispensed with at the table and salad oil substituted. A good brand of oleomargarin is cheaper than butter and much better than butter of the second grade. The demands upon the fat resources of the United States today are enormous.

The salts of milk are desirable for the protection of the reserves of the salts of the body. A diet of bread and milk, however, which is the basic diet of the Russian peasant, yields a urine which deposits uric acid. Addition of potatoes to this diet gives alkali, which causes the excretion of a less acid urine and one capable of holding uric acid in solution. Milk is poor in iron, and so this element may be furnished in green vegetables or in spinach or in fruits, such as grapes and raisins.

One of the simplest dietaries known is that of the Italian peasants of southern Italy. Some of them have lived on cornmeal made into "polenta" or into corn bread, eaten with cabbage

or beet-tops, taken with olive oil, which has been flavored with garlic or Spanish pepper. This has been the fundamental diet for generations. Just as in the case of the modern experimental biologic analysis of a balanced ration in which such a ration is given to rats and its efficiency as a diet is tested by its capacity to support normal growth and reproduction of the species, so here the experimental evidence is presented that corn, the cheapest of the cereals, olive oil, a cheap vegetable fat, may become a sustaining diet when green leaves are a supplementary factor. The work of McCollum shows that the green leaves contain proteins which supplement the inferior quality of the protein in corn, contain salts similar to those found in milk, and also contain the fat-soluble and water-soluble "vitamins" which are found in milk.

It is evident that a proper diet can be planned only after the consideration of a variety of factors. Fortunately, man instinctively demands variety in his food and instinctively takes that quantity of nourishment which maintains him in an equilibrium of substance year after year. In cases where too much food is taken he gains in weight, and where too little food is taken he loses in weight. Gain or loss of body fat is entirely dependent upon whether the quantity of food-fuel ingested is more or less than that needed.

Tables showing the cost of various wholesome food-stuffs about July 1, 1917, are here reproduced for the benefit of the reader. The tables were prepared by Dr. F. C. Gephart and issued by the Department of Health of the City of New York in a leaflet edited by Doctors Holt, La Fetra, Pisek, and Lusk on the subject of food for children. If the world is seeking after energy in the form of food-fuel, the world is rightly entitled to understand the value of its purchases. It must be clearly understood that people are always destined to look with hopeful anticipation toward the enjoyment of a meal. They will instinctively "eat calories" just as they instinctively "eat pounds." They *buy pounds* of food, and they could buy more intelligently if they knew the energy value of what they buy.

	Cost of 1000 calories, cents.	Price per pound, cents.
TABLE 1—*Cost of Fats.*		
Cottonseed oil	7.3	31
Oleomargarin	8.5	30
Peanut butter	8.8	25
Butter	11.9	43
Olive oil	12.1	51
Bacon	13.8	37
Bacon, sliced, in jars	23.8	65
Cream (extra heavy, 40 per cent.)	37.7	65 (1 pint)
TABLE 2—*Cost of Cereals.*		
Cornmeal, in bulk	3.6	6
Hominy, in bulk	3.6	6
Broken rice, in bulk	3.7	6
Oatmeal, in bulk	3.8	7
Samp, in bulk	4.2	7
Quaker Oats, in package	4.4	8
Macaroni, in package	4.5	8
Wheat flour, in bulk	4.6	8
Malt breakfast food, in package	4.8	8
Pettijohn, in package	5.3	9
Cream of Wheat, in package	5.7	10
Farina, in package	5.9	10
Cracked wheat, in bulk	5.9	10
Pearl barley, in package	6.0	10
Barley flour, in bulk	6.1	10
Whole rice, in bulk	6.1	10
Wheatena, in package	8.1	14
TABLE 3—*Cost of Ready-to-serve Cereals.*		
Shredded Wheat Biscuit	7.8	13
Grape-nuts	8.6	15
Force	9.4	16
Corn Flakes	11.7	20
Puffed rice	23.5	38
TABLE 4—*Cost of Vegetables.*		
White potatoes	12.9	4.0
Turnips	20.0	2.5
New beets	27.6	5.0
Onions	29.3	6.0
Spinach	30.0	3.3
Green peas	39.2	10.0
Lima beans	39.2	10.0
Cauliflower	42.9	6.0
Carrots	50.0	8.0
String beans	55.6	10.0
Squash	76.2	8.0
Lettuce	89.4	7.0
Celery	214.0	15.0

	Cost of 1000 calories, cents.	Price per pound, cents.
TABLE 5—*Cost of Breadstuffs.*		
Ginger snaps	6.3	12.0
Graham bread	8.2	10.3
White bread	8.5	10.3
Rye bread	8.7	10.3
Graham crackers	9.2	18.0
Soda crackers	9.4	18.0
French rolls	10.8	14.0
Uneeda Biscuit	12.4	24.0
TABLE 6—*Cost of Proteins.*		
Milk (Grade A)	20.0	13.0 (1 quart)
Roast beef (rib)	23.4	26.0
Buttermilk	26.5	9.0 (1 quart)
Lamb chops (loin)	32.7	43.0
Lamb chops (rib)	34.9	38.0
Young codfish (fresh)	38.6	12.0
Chicken (roasting)	41.3	32.0
Eggs	44.7	45.0 (1 dozen)
Beefsteak (round)	50.4	34.0
TABLE 7—*Cost of Fruit.*		
Fresh (in season):		
Bananas	23.0	6
Apples	23.7	5
Oranges	65.0	10
Dried:		
Prunes	8.4	10
Apples	11.1	15
Peaches	12.5	15
Apricots	15.5	20
TABLE 8—*Cost of Syrup.*		
Karo corn syrup	5.7	8

In conclusion, it may be of interest to summarize the variations in the basal metabolism in various diseases, the further details and references concerning which may be found elsewhere.[1]

In *acromegaly* the basal metabolism is increased (Magnus-Levy), whereas in *dystrophia adiposogenitalis* it is decreased (Means). In cases of *obesity* in which the pituitary is not involved there is no change in the level of the basal metabolism (Means).

In severe cases of *carcinoma* the heat production may be 30 or 40 per cent. above the normal (Wallersteiner).

[1] Lusk, G.: The Elements of the Science of Nutrition, Philadelphia, 1917, 3d ed.

In patients with *cardiac disease* with compensated cardiac lesions or mild nephritis the basal metabolism is normal, but when dyspnea is present it may rise to between 25 and 50 per cent. above the normal (Peabody, Meyer, and DuBois). In like manner, in simple *anemia* there is no change in metabolism, but when the hemoglobin content of the blood falls to 20 per cent. in severe *pernicious anemia*, the metabolism may be 24 per cent. above the normal (Meyer and DuBois). In *chlorosis* there is no change in the basal metabolism (Rolly).

In *lymphatic leukemia* the metabolism is greatly increased (Grafe), and vigorous *x*-ray treatment, though largely reducing the number of leukocytes, does not alter the metabolism (Murphy, Means, and Aub).

In cases of *gout* the basal metabolism is normal (Magnus-Levy) and also in cases of *stupor* (Grafe).

In *diabetes* the metabolism is sometimes higher and sometimes lower than the level of the basal metabolism (Allen and DuBois). It has been found to be markedly higher in a case in which the protein metabolism was abnormally high (Geyelin and DuBois).

In *emaciation* the basal metabolism falls greatly. A nervous invalid, who reduced his weight 30 per cent. (115 to 79 pounds), and who was literally "skin and bones," had a metabolism which was 33 per cent. below the normal for his height and weight. In the case of a woman who had lost half her weight the reduction in metabolism was 37 per cent. She was near the border-line of death from starvation (Allen and DuBois). This factor has to be considered in discussing the height of the basal metabolism in wasting disease. The last-named individual required only 40 per cent. of the food intake which was necessary to maintain her before the reduction in weight. Loss of body weight reduces the basal metabolism, reduces the quantity of food-fuel necessary to transport the body in walking, but does not change the requirement of energy necessary to accomplish a given amount of muscular work.

A modification in the secretion of the thyroid gland profoundly affects the amount of general metabolism. In *cretinism*, an example of hypothyroidism, the basal metabolism may be

20 per cent. lower than the normal (DuBois). In the hyperthyroidism present in *exophthalmic goiter* DuBois finds that the height of the basal metabolism is the best index of the severity of the disease and classifies his cases as follows:

> Very severe, showing increases of 75 per cent. and more.
> Severe, showing increases of 50 per cent. and more.
> Mild, showing increases of less than 50 per cent.

In very severe cases the heat production may rise to nearly double the normal value. The specific dynamic action of protein ingested falls within the normal limits.

Finally, in *fever* the heat production is largely increased and also the metabolism of body protein. The best method of protecting the waste of body protein is to give carbohydrate in large quantity (Shaffer and Coleman), but this does not prevent the toxic waste of body protein in infectious fever (Coleman and DuBois). In *typhoid fever* the increase in basal metabolism is about 40 per cent. and may rise to 50 per cent. above the normal. The ingestion of protein in considerable amount does not increase the level of metabolism in this disease. During the second, third, and fourth weeks of convalescence the basal metabolism may be 15 per cent. above the normal level; this period is that of the regeneration and repair of the muscle tissue, and DuBois has compared it to the corresponding period of high metabolism during adolescence. In the chill in *malaria*, or in that which follows intravenous injection of typhoid vaccine, there is a sudden rise of body temperature and a sudden increase in heat production. The quantity of heat lost from the body by the usual means of radiation and conduction and by water evaporation is, however, unchanged from the normal by the chill. Hence, the heat produced by the chill is stored in the body and lifts the body temperature to a higher level (unpublished work of Barr, Cecil, and DuBois).

Since the total energy for the maintenance of our bodies can be measured in calories, and since this energy serves for the maintenance of the peoples of the world, is it not surprising how little even educated people know about the subject?

CLINIC OF DR. MAX EINHORN

POST-GRADUATE MEDICAL SCHOOL

THE DIET IN DISEASES OF THE KIDNEYS

THE kidneys are entrusted by the organism with two very important functions: (1) to excrete waste products, unnecessary material and superfluous fluids (water) from the body; (2) to retain all material valuable to the system. The blood in passing through the glomeruli is subjected to a scrutinous examination by the renal cells, and the double function just mentioned is in this way carried out.

In disturbances of the kidneys two sets of phenomena are noticeable: (*a*) accumulation in the blood of substances which should have been eliminated; (*b*) excretion from the blood of material that should have been retained.

The symptoms encountered in renal affections are all more or less dependent upon the above two factors, which are present either in association with each other or separately. The gravity of the disease is likewise subject to the extent of functional failure in these two directions.

Alimentation, which consists in the introduction and working up of new nutritive material, manifestly increases the difficulties against which the kidneys have to battle. The importance of diet has, therefore, always been recognized as one of the principal factors in the treatment of renal affections.

I chose this subject for discussion on account of the many interesting points it presents to the clinician.

The views regarding the diet of nephritis have undergone many changes in the course of the last century. At first it was generally believed that the main object of diet should consist in replenishing the lost albumin, and for this reason richly protein foods (meats)

were given. Soon, however, it was discovered that under this régime the nephritics did not show the desired improvement, and rather became worse. This led to the selection of a diet containing very little protein, and as such, milk was recommended. This valuable food still forms the mainstay in this disease.

If we take into consideration the great variety of symptoms met with in nephritics, it is at once clear that one and the same diet will not fit every case. Thus a patient with edematous swellings all over and chlorid of sodium retention will require a salt-free diet and restriction of fluid, while another, with almost natural water and chlorid of sodium excretion, will be able to take fluids and a moderate amount of salt.

With regard to diet, the affections of the kidneys will have to be divided into the following groups:

1. Acute conditions:
   (Nephritis acuta), including exacerbations of chronic states.
2. Chronic affections:
   (*a*) Parenchymatous nephritis,
   (*b*) Interstitial nephritis,
   (*c*) Congestive nephritis.
3. Complications:
   (*a*) Uremia,
   (*b*) Dropsy.

1. In **acute nephritis** (sudden onset of disease, edematous swellings, diminished urinary secretion, much albumin, casts, etc.), including exacerbations of the chronic kidney lesions (which present similar symptoms), the diet and, in fact, the entire plan of treatment is guided by the principle of rest. Milk, gruels, and mineral or plain water are given in quantities of about 150 c.c. (℥v) every two hours or so. If cows' milk is not well borne, a vegetable milk (prepared of nuts or sweet almonds) may be given instead. Meat soups (containing extractive material) and foods rich in protein are forbidden. Lemonade and fruit juices may be given. The work of the kidney is reduced to a minimum and its function partially replaced by other eliminative organs (skin and intestine). With this object

in view, the diet can be of assistance. Hot drinks, even in small quantities, like lemonade or weak tea, will act as a sudorific, while fruits (containing organic acids) will increase the intestinal activity. As soon as the acute symptoms begin to subside, the diet should be increased. The latter also applies to acute conditions lasting a longer time (ten days, two to three weeks, etc.). Here likewise more food should be given. The patients are fed on milk, gruels, porridges, bread, 2 to 3 eggs (boiled or scrambled) daily, and fruits. As little salt and seasoning as possible should be permitted in the diet.

Still later a small quantity of meat is added. In case there is complete recovery, a return to the common foods is permissible; if, however, the disease is taking a chronic course, the diet, which will be described in the following, must be observed.

2. The diet in **chronic affections of the kidneys:** (*a*) Chronic parenchymatous nephritis (face pale and edematous, urine of moderately light specific gravity containing albumin and casts).

This forms a class of cases in which a great many practitioners prescribe a milk diet and keep it up indefinitely. While milk presents an ideal food for these patients and may be used with advantage for a week or two at a time, it should not form the only means of nourishment for a prolonged time. Although the kidneys are given more rest under this régime, the organism suffers from this one-sided and at times insufficient alimentation. The anemia here generally present is enhanced, and thus the conditions are unfavorable for the recuperation of any diseased organ. The consequence is that the kidney, notwithstanding its diminished activity, does not recover. A more liberal diet, although requiring more strenuous work from the kidney, creates a more healthful state of the individual and gives the affected organ a better chance for recovery.

The daily diet will, therefore, consist of the following:

Milk or koumiss, about 1 quart, gruel or porridge, about 1 pint (given in two portions), 2 to 3 eggs (soft boiled, scrambled, or poached), tender meat, preferably the white kinds (about 3 to 4 ounces), bread and butter; weak tea or weak coffee with sugar; light vegetables and fruits. Table salt should be avoided, and

the dishes prepared, if possible, without salt; seasoning substances—pepper, onion, mustard, and the like—should likewise be avoided. Meat soups and broths should be forbidden. The amount of fluid, including that contained in the food, should not be more than 2½ quarts in twenty-four hours.

Great variety in the selection and preparation of the foods is very desirable, for the appetite of the nephritic is usually poor and requires as much stimulation as possible. The patients should be encouraged to eat, and everything should be done to raise the nutritive state of the organism.

(*b*) Chronic interstitial nephritis (patient usually well nourished, with a florid complexion and high-strung temperament; urine pale, abundant in quantity, of a diminished specific gravity, with little albumin and but few casts, and sufficient sodium chlorid excretion; the blood-pressure is usually high).

This form of nephritis is frequently encountered in plethoric and stout individuals. Luxurious living, high tension in business or professional activities, and diminished mental rest as well as lessened muscular exercises greatly contribute toward the development of interstitial nephritis. Tobacco and alcohol are here also contributory factors.

The dietary régime will be of a restricting type. Simple foods in moderate quantities, with but scanty protein, should be given. Purin-containing aliments, alcoholic beverages, and spices should be prohibited. The physician will have to guard the patient against taking too large an amount of food. In fact, reduction in the body weight is in this class of cases frequently beneficial. The daily ration may consist of white meat (chicken or fish) ʒiiiss, 1 or 2 eggs, some salt-free bread and butter, vegetables, fruits, and 1 to 2 glassfuls of milk. Alcoholic beverages, coffee, and meat broths should be forbidden; while alkaline mineral waters and a moderate quantity of weak tea may be given.

Occasionally it is advisable to institute one or two meat-free days weekly and also to prescrbe a very small breakfast (½ roll and 1 cup of weak tea without milk). Provided the quantity of foods taken at the other two meals is not increased, this plan

of alimentation will lead to a slight reduction in weight. Wherever the latter appears desirable, this régime can be applied with advantage.

(*c*) Congestive nephritis (scanty urine of high specific gravity containing a small amount of albumin, without any or but very few casts).

Congestive nephritis is usually due to grave disturbances of the heart, leading to diminished pressure in the renal arteries and increased pressure in the corresponding veins. The treatment must be directed toward improving the general circulatory system and the diet will be that adapted for the special heart lesion.

The main principle is to select a diet suitable for rest of the kidneys—as little protein as possible, no irritating substances, a small amount of fluid. Karell's diet is here appropriate for about three to five days. Later, especially if the condition improves, the diet is gradually and cautiously increased.

3. **Complications.**—(*a*) Uremia; (*b*) Dropsy.

(*a*) *Uremia.*—The diminution of the excretory function of the kidneys leads—if pronounced, already at the beginning of the disease, otherwise in the later stages—to uremia. The latter manifests itself when present in a minor degree by slight headaches, nausea, sometimes accompanied by vomiting and general uneasiness. When the excretory function is lacking in a higher degree, it leads to loss of consciousness and also convulsions. The arterial blood-pressure—usually high in nephritics—frequently shows a further increase; although in rare instances the reverse takes place (bad prognosis).

The diet will consist of milk and gruels and fruit juices, 5 to 7 ounces every two to three hours. When vomiting exists or when loss of consciousness is present, rectal alimentation must be resorted to. Notwithstanding the existence of edema, a 5 to 6 per cent. glucose solution can be given by the Murphy drip through the rectum in quantities of 1 to 2 quarts daily. By this means it is occasionally possible to stimulate the kidneys to better work, in such a manner that the obnoxious substances are ultimately removed, leading to a return of consciousness.

As soon as patient is able to take food, the same diet is employed as in acute nephritis. Provided there is a further improvement, alimentation is gradually increased and the rules laid down in chronic kidney disease observed.

(*b*) *Dropsy* (general edematous swelling, anasarca, ascites, pleuritic effusions) frequently appears in acute nephritis and is almost always encountered, at one time or another, during the chronic stage of renal affections. This complication requires special treatment and diet. An exclusive milk diet ($1\frac{1}{2}$ to $2\frac{1}{2}$ quarts daily) is frequently found beneficial, the urine becoming more abundant, showing less albumin, and the swellings gradually disappearing. The general nutrition, however, cannot improve on this insufficient alimentation. For this reason this régime, while useful for a short period of time, cannot be employed indefinitely.

Widal and Strauss have conclusively shown that chlorid of sodium retention, which is frequently met with in nephritis, leads to edema. This discovery gave origin to a new mode of diet appropriate for these cases, namely, the salt-free diet. Restriction of fluids and of chlorid of sodium is most important. The diet consists of bread, milk, eggs, arrowroot, rice, vegetables; everything prepared without salt. Fish, poultry, or meat may be added, and milk (if not desired) entirely omitted from the bill-of-fare. The quantity of meat should, however, not exceed $\frac{1}{4}$ pound a day. Fruits should be given in considerable quantities. while spices and meat soups, likewise alcoholic beverages, should be entirely forbidden. The salt-free diet régime has been generally accepted and is employed with great benefit.

Another mode of dietary régime for dropsy has been suggested by Kakowski.[1] This eminent clinician gives his patients 3 to 5 pounds of squash daily divided into three portions, prepared with milk or cream or rice soup and butter. The squash is prepared as follows:

Raw squash, in quantities of 3 to 5 pounds, is cut into small pieces and placed in a pot, a small quantity of water, enough

[1] A. Kakowski: "Die Kürbisbehandlung der Ödeme," Zeitschr. f. phys. und diätetische Therapie, Juni und Juli, 1914, Bd. xviii, H. 6, 7.

to cover the bottom, is added, and the whole mass stirred. The pot is now left boiling over a low fire for two hours, and the contents are frequently stirred. The squash mush is then mixed with some butter and milk-soup (usually rice soup) and is ready for use. Instead of water the squash may be prepared with cream, which gives it a better flavor and makes it more nutritious.

Kakowski had excellent results from this exclusive squash régime. He considers the squash as the best natural diuretic, increasing the secretory function of the kidney without having any slight irritative effect on this organ.

In conjunction with Dr. N. Stadtmüller I have employed squash and also muskmelons, watermelons, and cucumbers in cases of dropsy. While we did not see as striking results as described by Kakowski, we, nevertheless, had the impression that this group of fruits (cucurbitæ) acts beneficially on the kidney function and deserves recommendation. The squash we gave as prescribed by Kakowski. Musk- and watermelons we employed raw (about 2 pounds daily), taken in conjunction with a salt-free diet. The cucumbers were given as a vegetable, boiled in milk, about 1 pound daily, also in conjunction with a salt-free diet.

Squash, melons, and cucumbers may be administered with advantage not only in cases of dropsy, but in all instances of kidney derangement. The beneficial action of the cucurbitaceæ may be explained by their richness in potassium salts while containing but little chlorid of sodium, and also by their mild aperient qualities.

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APPARENT AND REAL APPETITE DEFECTS IN THE YOUNG

Actual and Apparent Absence of Desire for Food in the Infant at the Breast, the Bottle-fed Baby, and in the Young of All Ages. Causes and Various Types. Proper Regulation of Diets, and Treatment of Some of the Causes and Existing Conditions.

AMONG the minor troubles in the young for which the pediatrist and general practitioner are often consulted is an absence of desire for food. We are confronted with this problem in the infant at the breast, in the bottle-fed, and from this period upward we find cases at all ages of early childhood.

All well children when fed on suitable food at right intervals are ready for the suitable food at right intervals. It is understood, of course, that a sick baby from whatever cause may refuse his food whether supplied by the breast or bottle. The patients that we are dealing with are the apparently well, suffering from no ailment, the only complaint is that the child refuses to take adequate food. A well baby, one that has been a strong and ready nurser, develops a disinclination to take the breast. If urged, he takes the nipple indifferently and is apparently easily satisfied. I have found this condition due in the majority of cases to too frequent nursings. Not infrequently these infants are being nursed at two-hour intervals during the day and two or more times during the night. A safe nursing rule even in the very delicate is a three-hour interval during the day and one feeding at night until the third month is completed. Satisfactory feeding hours I have found to be as follows: 6 and 9 A. M., 12 M.,

3, 6, and 10 P. M., and 2 A. M. The 2 A. M. nursing may be discontinued with advantage at the completion of the second month in vigorous nursers that have the advantage of a good milk-supply. After the third month in all well infants there should be but six nursings, as follows: 6 and 9 A. M., 12 M., and 3, 6, and 10 P. M. After the fifth month in many, and after the sixth month in practically all, there should be but five nursings in twenty-four hours, as follows: 6 and 10 A. M., 2, 6, and 10 P. M. Time and again I have known infants to refuse the breast after some severe mental shock in the mother. The occasion for the mental disturbance may be known only to the mother, and she may not always care to have it known. Domestic upheavals of various natures are not unknown in the family circle and may be the occasion of a change in the milk-supply, which the child always appreciates. I have known infants to be made acutely ill under such circumstances. Infants will sometimes refuse the breast or nurse very indifferently upon the advent of menstruation in the mother or wet-nurse.

In a vigorous, overfed mother of the inactive type the milk may be of a high fat content, the infant is fed beyond his capacity and requirements, and is accordingly not hungry. I have repeatedly had infants brought to me because of apparently indifferent appetite, with stationary or loss of weight, with the story that the baby would nurse vigorously for a few minutes and then stop and refuse the breast. Examination into such cases has shown that the child has drained the breast and refuses to pay further attention to a dry nipple.

When babies refuse to nurse it is always well to test out the milk-supply with a breast-pump to find out if there is sufficient milk to encourage the child in his efforts.

A mother is told by the doctor or nurse to nurse her baby for twenty minutes. He nurses but four or five minutes and resists all further persuasion, although there is plenty of milk to be had. This baby should be weighed before and after nursing a few times. It will often be found that he has gotten all he can hold—3 to 5 ounces. In vigorous nursers with a free supply 1 ounce may be taken every minute.

The Bottle Fed.—The above regulatons as regards frequency of feedings applies to the bottle fed also. In fact, the long-interval feeding is more necessary in indifferent bottle feeders than in the breast fed.

There are many possibilities for the production of indifferent appetite, apparent or real, in the bottle fed. Local changes in the nasal passage, abrasion of the mouth or fissures of the lips will have less effect on the bottle-fed than on the breast-fed baby because, as a rule, the breast-fed baby has to work harder for his food. Nevertheless, I have repeatedly known bottle-fed babies to resist attempts at feeding because of the pain attendant upon the process. This is particularly the case in gingivitis and stomatitis. Occasionally the eruption of a tooth will cause sufficient local discomfort to interfere with the taking of the nipple. The child may refuse the nipple because it is too free and the milk chokes him. This is usually readily appreciated and remedied. He may likewise refuse it because it is too slow (this is much more frequently the case) and he becomes discouraged in the attempt to satisfy his hunger, a difficulty readily remedied. The child may refuse the bottle because the milk is too hot or too cold—100° to 105° F. is a suitable temperature. High fat and high sugar are very frequent causes of loss of appetite. Food with high fat content is slow in leaving the stomach. The formula should not contain more than 4 per cent. of butter-fat or more than 7 per cent. of sugar, regardless of the age of the patient. There are infants who have a low fat capacity and who will take and thrive on a 2 per cent. fat mixture, when a 4 per cent. mixture will cause loss of appetite if not illness. A sugar content above 7 per cent. will almost invariably produce loss of appetite if long continued.

The persistent feeding of an excessive quantity of a milk mixture will invariably produce indifferent desire for the bottle. It is a fairly safe assertion that the giving of too strong food at right intervals or the giving of any food at too frequent intervals are the chief causes of indifferent appetite in the bottle fed.

The mouth of every indifferent breast or bottle-fed child should be examined for sprue or abrasion or ulcers of the mucous mem-

branes of the buccal cavity. Fissures at the angle of the mouth and lips are very painful and will interfere with right feeding. Acute infections of the nasal passages, known as coryza and head colds, will cause a narrowing or closing of the nasal passage so as to make either bottle or breast feeding of no little difficulty to the infant.

Defective or so-called poor appetite in older children claims a great deal of our attention. These patients may be divided into three fairly distinct types: First, we have the habitually poor feeder. He was not keen on appetite as a baby. Mealtimes have always been a sore trial in the family. As often as the child is fed, just so often is the propaganda of coaxing, urging, and threats gone through with. This type of child is almost always constipated. He is undersized and underweight and there is a moderate secondary anemia. He is apt to be a bit precocious, overactive, usually spoiled, and of a whining, unhappy disposition. These patients are very difficult to treat, not a few of them being the only child, and the only child is particularly difficult when he has gotten into very bad bodily and mental habits.

Very good results may only be obtained when the full co-operation of the entire family is secured. The first and often most difficult thing to do is to dismiss the old nurse, who has perhaps brought up the father or mother and who has had the child from early infancy. It is quite necessary that the child be taken out of such control, as the old family nurse is usually more spoiled than the patient. Having placed the family where they belong, in the background, and given the child in charge of a competent young nurse, who has shown unusual capacity for such work, we are ready for detailed directions.

The child we will assume is between two and eight years of age. He may be older or younger, but rarely is younger than two years. He is given three meals a day with absolutely nothing between meals. The breakfast is given at 7.30 A. M., in bed. Cereals, milk, eggs, bacon, and bread-stuffs comprise the dietary. As wide a variety as possible in cereals is used, thus oatmeal, cornmeal, hominy, rice, and wheatena are allowed. Do not

be guilty of ever writing on a diet schedule or anywhere, or of telling the mother or nurse "cereals to be thoroughly cooked." This will be interpreted as meaning anything from one-half hour to six hours. The above cereals except rice should be cooked in water four hours the day before they are used, and the portion allowed warmed the following morning. Rice should be boiled in water six hours. The cereals are not always to be served in the same way. They may be served with milk and sugar (scanty) or butter and maple syrup, or the portion of a banana cut up with the cereal with milk over it. Cereals are often most difficult to give this type of child. I have always a great deal of sympathy for the unhappy youngster who has the cereal portioned out to him the selfsame way day after day. In addition to the cereal he is given an egg, not always soft boiled. It may be scrambled or poached. The following day he is given bacon with a different cereal, and the next morning minced white meat of chicken on toast and a different cereal served in a different way from the preceding morning. He is given milk or cocoa or malted milk and some kind of bread-stuff. In order to curtail his energy output he is kept in bed until 9.30 A. M. He is then allowed to get up, and is out-of-doors until 12.30, which is the dinner hour. At dinner he is given baked or broiled meats, poultry or fish, potato or rice, usually baked, and a green vegetable. As a dessert he is given a simple pudding or stewed fruit. A bread of some sort is given with each meal. After the dinner the child rests for an hour. He is then up and about in the usual childish fashion until 5.30 P. M., when he is bathed. At 6 P. M. supper is served. This consists of a cereal, farina or cream of wheat, or one of the cereals suggested for breakfast, and served in like manner. Occasionally a broth, chicken or mutton, may be given at the evening meal. After the fourth year baked potato is allowed. Many children enjoy cream cheese. Custard, cornstarch, and junket help to supply variety. When broth is given, stewed fruit will be acceptable. Milk is usually given at this time, or malted milk or cocoa. The milk and soup should not be given at the same time. Toast, dinner biscuit, or wheatsworth biscuit should always be offered. Most children enjoy a little honey

occasionally. A wide variety of foods should be on the permissible list.

Foods and feeding should never be discussed before the patient. He is given food at regular intervals, and if he refuses he is not urged, but nothing is given until the next meal. This should be an invariable rule. Patients of this type will often take the meat or egg readily, but will refuse vegetables, or they will take the potato and refuse everything else. The meat, potato, and vegetables are to be taken in rotation or not at all. The patient is never to be told stories at mealtime or coaxed by giving mouthfuls for the coachman, the cook, the little wooden horse on the table, or the policeman. In some cases it will be found advisable to stimulate the appetite by the use of drugs. If such is the case, 2 drops each of tincture of nux vomica and diluted hydrochloric acid in sweetened water may be given at two-hour intervals during the day. The management as outlined is what I have found necessary in treating these troublesome cases. Special nurses are not practicable in many instances. The mother or any sensible person may very easily carry out the suggestions offered if they are sufficiently interested and possess the necessary force of character. Under right management I have repeatedly known these cases to gain from 4 to 6 pounds the first month.

The second type is the child who is well nourished and will eat plenty if the stage settings are satisfactory. He demands that one person be present or demands an audience, and craves coaxing and attention and refuses food unless such attenion be supplied. I have seen time and again a company of dolls so arranged as to form a dinner party. The host sits at the head of the table, and all the dolls, the donkey, and the teddy bear propped up in chairs share the meal with the spoiled only child. Such a performance takes place with the first-born, rarely with the second, and never with the third.

The management of these children is to cut out the superfluous attention and allow them to get sufficiently hungry by allowing them to go without a meal or two.

The third type is the child who hates this, that, or the other

food. He is on a self-restricted diet as regards variety. In this class we find the milk drinkers, whose entire diet consists of milk and a few other foods. Such a boy was brought to me a few years ago. He was six years old and was taking 4 quarts of milk a day which was the sole dietary except bread and a little cereal. He was pale, sallow, pot-bellied, underheight and underweight, and constipated, so that he required enemata daily. The story in these cases of milk habit is that the child would take no other or very little other foods and had to have something. Others of this group will exist largely on meat because they will take but little other foods. One patient subsisted largely on oatmeal. Patients of this type are very apt to show severe digestive derangements. They have dilated stomachs and badly deranged intestines. They suffer from constipation and flatulence. The colon is apt to be dilated and ptosed. The bad dietetic habits are usually easily corrected, but the gastrointestinal tract responds but slowly to proper management. Of primary importance for right digestion and assimilation and right structural and physiologic development in children is a wide variety in the diet in which so-called roughage plays an important part.

In these cases I remove from the diet all the particular foods which have comprised the sole diet and give a diet suitable for the child's age. A point that you are to remember in all these freakish feeders is that the child will never hold out in his determination. The pangs of hunger bring man and beast to their knees.

Practically all of the patients of these groups are constipated. One free evacuation daily is provided for. I usually give sufficient aromatic cascara sagrada, fluidextract, three times a day after meals, to produce one or two evacuations daily. Any other simple laxative will answer if it will produce results. The diet, of course, is arranged along lines to remedy this complication.

These patients with defective appetite are not to be confused with those suffering from hyperchlorhydria, a not uncommon condition in children. In these cases there will be a loss of appetite or the appetite will occasionally be voracious, the child

not being able to wait until mealtime. He starts in vigorously, but his appetite is very soon appeased and he takes but a small quantity of food. In such cases there will be discomfort, eructations of gas, and the usual symptoms peculiar to this disorder.

Regardless of type there are certain conditions which may exist that might have an unfavorable influence on appetite and which must be removed. Enlarged tonsils and adenoids or adenoids alone have been a cause of poor appetite in many a run-about child. Anxiety as to school work in older children has had an unfavorable influence on appetite and, accordingly, on growth and development in not a few cases. Decayed teeth and sore gums must always receive attention in every child, sick or well, In the apparently well they may have much to do with defective eating. One feature is common in the majority of these cases, the patient is the only child or the only boy or the only girl in a family of three or more children.

CONTRIBUTION BY DR. WARREN COLEMAN

THE TYPHOID DIET

Historical; Principle of the High Calory Diet; Calculation of Diet; Quantity of Food; Administration of the High Calory Diet; Cautions; Food List; Food Combinations and Mênus for Various Cases and Complications; Control of Diarrhea by Increase of Fat; Patient with Intestinal Hemorrhage; Diet During Convalescence; Beneficial Effects of High Calory Diet.

Historical.—Hippocrates tells us that "in the ancient method of treating fever and febrile affections three main objects appear to have been kept in view; . . . third, to support the strength by a suitable supply of such nutriment as the system is then capable of receiving." He does not state, however, what the "ancients" considered "a suitable supply" of nutriment.

In Hippocrates' own time there were wide differences of opinion with respect to the diet of the fever patient. Some physicians advocated absolute starvation throughout the whole, or at least part, of the fever; others, including Hippocrates, considered food essential. Hippocrates thought it "disgraceful not to recognize a patient whose debility is connected with inanition. . . . Such mistakes of practitioners are particularly ridiculed by mankind," for another physician or private person, coming in and giving food, "seems, as it were, to resuscitate the dead."

The Hippocratic diet consisted of barley gruel (there was much discussion whether it should be given strained or unstrained), acidulated honey (oxymel), honey boiled in water (hydromel), and sometimes wine. Hippocrates recognized that the nutritive value of honey was greater than that of wine.

He recommended that the gruel be given only once a day to patients who had been in the habit of taking only one meal, and twice to those taking two meals; the quantity was to be small at first and the gruel not very thick. It is obvious that the Hippocratic diet was little better than starvation.

According to Galen, Petronos gave flesh and wine to fever patients.

Coming down to more modern times, much interesting literature on the fever diet appeared in the early part of the nineteenth century. Graves is generally given credit for having popularized the practice of attempting to nourish the fever patient. Trousseau says of him, "When he inculcated the necessity of giving nourishment in long-continued pyrexias, the Dublin physician, singlehanded, assailed an opinion which appeared to be justified by the practice of all ages."

According to Graves the starvation treatment "sprang from the doctrines of those who maintained that fever depended on general or topical inflammation," and that, in consequence, the system must be reduced by depletion and low diet. "After the third or fourth day of fever I always prescribe mild nourishment, and this is steadily and perseveringly continued through the whole course of the disease," Graves said.

Graves' diet consisted of well-boiled gruel made of groats and flavored with sugar; a tablespoonful of toast crumbs, treated with boiling water, given two or three times a day, arrowroot, and, as the fever advanced, mild animal jelly or broth. Beer, ale, porter, and wine were given to some patients. Graves thought that the popular practice of indulging patients in grapes and oranges was very hazardous; that stewed and roasted apples were still more dangerous. Yet when it is recalled that a good-sized orange furnishes approximately 100 calories, and that apples and grapes are quite nutritious, it seems likely that the patients taking fruit received more energy than those on Graves' diet.

Bright and Addison recommended that an attempt be made to nourish and support the patient, and advised beef-tea, wine, arrowroot, yolk of egg with sherry and sugar, oranges, and sweet

fruits. The total quantity of food was to be regulated by its effect and the condition of the patient.

Contrary to the prevailing opinion, Elliotson thought fever patients had good digestions. The diet he recommended furnished considerably more energy than any diet of his time, or even considerably later. He considered milk one of the best foods for the fever patient, and gave as much as the patient could drink. He also used beef-tea in quantities up to 2 to 3 pints a day; arrowroot, sago, and rice with milk; generous quantities of wine (from 1 to 2 pints of Port, Maderia, and Sherry a day) and porter (a wineglass or two every few hours).

The more recent history of fever diets is well known and need not be referred to at this time.

The Principle of the High Calory Diet.—The underlying principle of the high calory diet is to supply the patient with sufficient food to cover his daily expenditure of energy. Except for an increased destruction of protein, the metabolic processes of the typhoid patient differ from normal chiefly in the rate of combustion. As in health, fresh supplies of fuel are constantly demanded. Likewise, as in health, if fresh supplies are not available, the reserves of the body are consumed, and in direct proportion to the deficiencies of the diet. In effect, any diet which does not cover the heat production allies starvation with the bacterial foes of the patient.

Calculation of Diet.—The food needs of a patient may be calculated on the basis of his weight or surface area; that is, as calories per kilogram per day, or calories per square meter of surface per hour. The latter method is the more accurate and, since the publication of the DuBois "height-weight" chart for estimating surface area, is as easy of application as the other. The chart and method of using it are given on p. 516.

The basal metabolism of the average healthy adult (measured some hours after the last food while lying absolutely quiet) forms the starting-point of the calculation. According to DuBois (averaging his own and others' experiments), the basal metabolism amounts to approximately 26 calories per kilogram per day, or 40 calories per square meter of body surface per hour. These

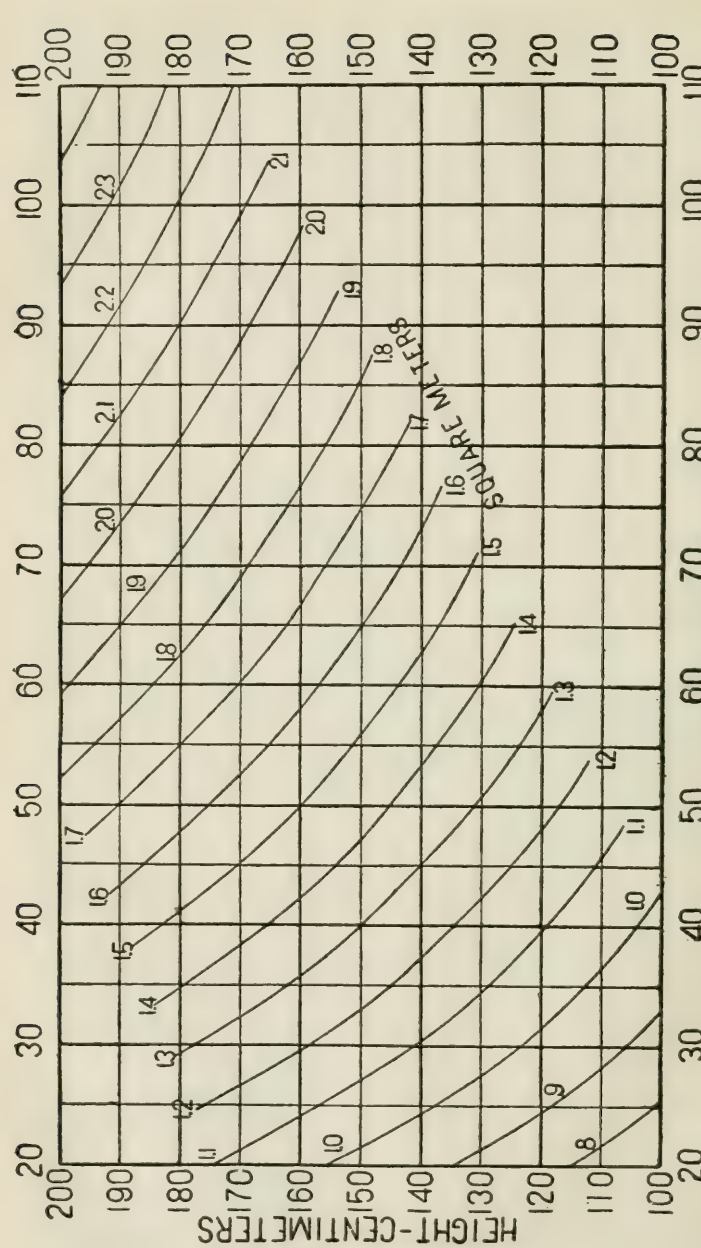

Fig. 45.—Chart for determining surface area of man in square meters from weight in kilograms and height in centimeters. The point of intersection of ordinate and abscissa for any individual is found and the surface area read off on the curved lines. For example, if a man is 150 centimeters in height and weighs 60 kilograms, his approximate surface area will be 1.55 square meters. (After DuBois and DuBois.)

figures must be corrected for special factors which raise the typhoid patient's metabolism over the normal basal level, viz., the increase due to the fever (averaging 40 per cent.), the stimulation of metabolism by the food ingested (3 per cent.), and the increase incident to the patient's muscular activity in moving about the bed (10 per cent.).

Taking these factors into consideration, the heat production of the average adult typhoid patient is found to approximate 40 calories per kilogram per day, or 60 calories per square meter of body surface per hour.

Boys about the age of puberty (twelve to thirteen years) have a basal metabolism which is 25 per cent. higher than that of adults (DuBois). Children between the ages of two and six years have a much higher, but as yet imperfectly ascertained, metabolism. After the age of six years the basal metabolism gradually falls until the twentieth year. Patients who are very restless may increase their metabolism 25 per cent. or more. When necessary, allowances should be made for the above factors in the calculation of diets.

It should be added that the figures given for the metabolism of the typhoid patient—viz., 40 calories per kilogram per day and 60 calories per square meter of surface area per hour—merely express the heat production. There is evidence that only so much food as will cover the heat production is not the optimum amount which may be given. This is because typhoid patients continue to lose nitrogen until the energy value of the ingested food reaches from 50 per cent. to more than 100 per cent. above the heat production. With this correction the typhoid patient's need for food is equivalent to 60 to 80 calories per kilogram per day or 90 to 120 calories per square meter of surface area per hour.

Quantity of Food.—The quantity of food which a patient should be given must be regulated by the patient's ability to utilize it. There is no more justification for injuring a patient with food than for injuring him with anything else.

If the patient's digestion is upset by the injudicious administration of food, and he vomits it or loses it in part through diar-

rhea, the very object of the high calory diet is defeated, namely, to supply the patient with sufficient food to cover his expenditure of energy.

It has been stated above that the actual heat production of the average adult typhoid patient is approximately 40 calories per kilogram per day or 60 calories per square meter of body surface per hour. No valid argument has yet been advanced to prove that a patient is benefited by receiving less than a corresponding amount of food.

The question has been raised, however, whether a patient should be given the excess of food over his heat production which is necessary to protect the body against loss of protein; that is, whether he should be given from 60 to 80 calories per kilogram per day or 90 to 120 calories per square meter of surface area per hour. Personally, I am convinced that he should. It cannot be doubted that a dietary which permits the loss of nitrogen by normal persons is inadequate, and I believe that the desirability of preventing such loss in fever is even more imperative than in health. Typhoid patients who lose nitrogen lose weight. For ten years it has been my practice to encourage typhoid patients to take all the food they could digest and absorb, and I am convinced from this experience that the patients who took the larger amounts of food came out of their illnesses in better condition.

The figures given above have been derived from the study of a large number of patients. In general, they represent averages. In practice we deal with individuals under conditions where it is impossible to measure the patient's metabolism, obtain the nitrogen balance, or accurately follow the weight. Another obstacle which confronts the physician is that different lots of the same foods may vary greatly in composition and, consequently, in energy value.

Without assistance from the laboratory in ascertaining the above-mentioned facts the physician must be guided solely by clinical considerations in the administration of the diet; that is, by the general condition of the patient, his weight, and whether he is hungry. The most important of these guides is the (esti-

mated) weight. If a patient is losing weight, he is surely not receiving sufficient food. The more nearly a patient is kept in weight equilibrium, the more certain it is that all of his nutritive requirements are being met.

The patient's appetite is not always a safe guide to his food needs. Loss of appetite is common in the earlier stages of the fever and may be disregarded, provided the food does not upset the patient's digestion. But when hunger appears, the question of increasing the patient's food must be met. Many of my patients have complained of hunger even when receiving 3000 and more calories a day. Under such circumstances I have always increased the food, and have never found cause to regret it. I tell all patients to ask for more food if they wish it; all nurses, to give the patient as much food as he is capable of digesting.

The amounts of food which patients will take vary with the stage of the disease. All patients take less in the earlier stages than in the later. Very few patients are able to take sufficient food in the period of level temperature to completely protect the body protein. The majority of patients lose some weight during this period. But by the time the steep-curve temperature phase arrives the appetite has usually returned—sometimes it has become voracious—and little difficulty will be experienced with the food. Usually by the end of the fever the lost weight will have been regained. Whenever a patient passes his normal weight the amount of food should be diminished.

Finally, it must be recognized that no patient can be given more food than he will take. He should not be given more than he is capable of digesting and absorbing. But throughout the disease the attempt should be made to give the patient his calculated requirement.

Administration of the High Calory Diet.—The physician who approaches the dietetic treatment of typhoid fever with the notion that the high calory diet implies the administration of a previously calculated number of calories is likely to fail. The caloric value of the food should be calculated at the end, rather than the beginning, of the day.

Success in the administration of the diet depends upon indi-

vidualization in the feeding. It is the patient, not the disease, which must be fed.

Typhoid fever does not alter the patient's preferences for foods or remove existing food idiosyncrasies. Foods which disagree with a person when he is well are not more likely to agree with him when he has typhoid. I would say, however, that there often exists a prejudice against milk which has no justification in fact.

As far as is consistent with the patient's temperament, he should be taken into the physician's confidence. The object sought in the administration of so much food should be explained to him. It is nearly always advisable to tell the patient that "the more he eats, the sooner he will get well." Often it is surprising to see the effect of such a statement upon the amount of food consumed. The patient may be consulted with respect to the kinds of food he prefers, and, as far as possible, they should be given to him. His food habits should always be taken into consideration.

The amount of food must be regulated by the patient's ability to utilize it. Aside from digestive disturbances, there is far greater probability of the patient receiving too little rather than too much food.

An important aid to the successful administration of the diet is a conscientious nurse or attendant. The principle involved should be explained to her. It is preferable, but not necessary, that she should understand the caloric values of the foods before coming on the case. However, the number of foods concerned is not great and their values can be quickly learned. It is desirable that the nurse keep an accurate record of the amounts of all foods which the patient takes. It is recommended that the physician frequently check up the nurse's calculations. This ensures exactness and gives encouragement and confidence to the nurse.

Unless the patient craves food, which is exceptional in the early stage of the disease, the amount administered during the first day or so should be relatively small. Whether it should be liquid or not depends upon the mental state of the patient.

If he is able to masticate thoroughly the more solid articles of food, there is no reason why he may not have them. If his nervous system has been overwhelmed by the virulence of the disease, the food should, of course, be wholly liquid.

After the first day or so the attempt should be made to increase the quantity of food. The rate at which the food may be increased must be determined for each patient. In many cases the increase may be made rapidly. In other cases it must be made gradually. But in all cases no opportunity to increase the food should be overlooked. The addition of even a teaspoonful of milk-sugar or cream is so much gain.

Cautions.—The only unpleasant effects which have been observed to arise during the administration of the high calory diet have affected the digestive tract. There have been nausea, or nausea and vomiting—occasionally vomiting without nausea—tympanites, and diarrhea. Which of these occur, or whether any of them, depends upon several factors: the food peculiarities of the patient, indiscretion in crowding the food too rapidly, or the too great preponderance of fat or carbohydrate. In the author's experience nausea and vomiting most often are caused by food mixtures which are too rich; for example, the milk, cream, lactose, and egg mixtures. Exceptionally, patients enjoy them and digest them perfectly. Sometimes large amounts of milk-sugar have caused vomiting without nausea. If vomiting should occur, the diet must be reduced to its simplest terms, or all food should be withheld for a time—usually a few hours suffice. On the other hand, when the vomiting seems not to be due to indiscretion in administration of the diet, and patients vomit the simplest articles, I have not hesitated to give food in the hope that some of it would escape through the pylorus and be utilized.

Perhaps a majority of patients taking the high calory diet have a moderate degree of abdominal distention. Usually it produces no discomfort and may be ignored. If it reaches proportions which cause distress and appears likely to increase the tendency to hemorrhage or perforation, it indicates some fault with the diet. The total amount of food may be greater

than the patient can handle, or the diet contains too much fat or too much carbohydrate. Occasionally eggs cause tympanites. If so, they should be eliminated from the dietary. An excess of lactose is the commonest cause of tympanities. Less often it is due to cream. Exceptionally it occurs whenever the attempt is made to carry the food beyond an amount representing 1000 to 1500 calories, irrspective of the proportions of the food-stuffs. In this case the tympanites is attributable to an unfavorable intestinal flora (Torrey).

Diarrhea is most often due to an excess of cream. Occasionally it is caused by lactose, although lactose has not been observed to possess the laxative properties which have been attributed to it.

The occurrence of diarrhea warrants the assumption that the diet is improperly arranged. In practically all instances diarrhea, whether it has pre-existed or develops under treatment, can be controlled by alteration of the diet. It is usual to begin by reducing the cream. If the diarrhea should persist or increases, it is probably due to lactose and not to fat—the lactose should be eliminated and the fats (especially cream) should be increased. In several such instances the author has controlled the diarrhea in this manner though the fat intake was raised to 200 to 300 grams a day.

The Bacillus acidophilus, which Dr. Torrey prepares in pure culture for therapeutic use at the author's suggestion, has been of assistance in hastening the transformation of an unfavorable intestinal flora and in thus controlling tympanites and diarrhea.

FOOD LIST[1]

The foods which the author has used most frequently are contained in the following table. The calory values given for most of the articles are approximate, but are sufficiently accurate for practical purposes.

[1] Modified from the list published in Amer. Jour. Med. Sci., 1912, cxliii, 77, to accord with the values employed in the Metabolism Ward of the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital.

Rubner's figures are universally employed for calculating the calory values of the several food-stuffs.

Protein (pure), 1 gram equals 4.1 calories.
Carbohydrate (pure), 1 gram equals 4.1 calories.
Fat (pure), 1 gram equals 9.3 calories.

Name.	Amount.	Calories.
Apple sauce[1]	1 ounce	30
Apple, pared and cored	1 medium, about	75
Bread, average slice	30 grams	80
Butter, one pat	13 grams, about	100
Cocoa, one rounding teaspoon	5 grams	25
Crackers, soda, one cracker	9 grams	36
Crackers, Uneeda, one cracker	6 grams	25
Cream (20 per cent.[2])	1 ounce (30 c.c.)	60
Egg	1 average size	75
Egg white	white of 1 egg	15
Egg yolk	yolk of 1 egg	60
Farina (cooked)	1 heaping tablespoonful	25–30
Lactose (milk-sugar)	1 heaping teaspoonful	40
Lactose (milk-sugar)	1 measured ounce, 18 grams	72
Lemon-juice	1 ounce	12
Milk (whole)	1 ounce	20
Orange	1 large	100
Orange-juice	1 ounce	15
Oatmeal (rolled oats, cooked)	1 heaping tablespoonful	36
Potato	1 medium	100
Rice (boiled)	1 heaping tablespoonful, about	60
Sugar, cane-	1 heaping teaspoonful	40
Sugar, cane-	1 level tablespoonful	56
Toast	average slice	80

Alcohol (which has an energy value of 7 calories to the gram) has not been included in the foregoing list of foods because it is not required by the great majority of patients. But at times it serves a useful purpose. I have had typhoid patients who persistently declined all food—who would simply shut their teeth when it was brought to them—but who would take whisky without objection. In such cases I have given as much as 2

[1] Cooked without sugar.

[2] Approximately the same as the top 4 ounces from a quart bottle of milk that has stood at least six hours. This is not heavy cream. To add lactose to milk, boil 15 grams (½ ounce) of lactose in 30 c.c. (1 ounce) of water; cool and add to milk.

ounces of whisky every three hours without the least sign of intoxication or other harmful effect. In other instances I have given whisky for the purpose of increasing the energy value of an inadequate diet. There is no doubt in my mind that alcohol is oxidized by typhoid patients with the liberation of energy, and that under such conditions alcohol may be regarded as a food.

FOOD COMBINATIONS AND MÉNUS

The following food combinations and ménus will be found of assistance in administering the high calory diet.[1]

For 1000 calories a day:	Calories.
Milk, 1 quart (1000 c.c.)	700
Cream, $1\frac{2}{3}$ ounces (50 c.c.)	100
Lactose, $1\frac{2}{3}$ ounces (50 grams)	200
This furnishes eight feedings, each containing:	
Milk, 4 ounces	80
Cream, 2 drams	15
Lactose, 6 grams	24
Or	
Eggs, 2	150
Lactose, 30 grams (1 ounce)	120
Sugar, 25 ($\frac{4}{5}$ ounce)	100
Milk, 800 c.c. ($26\frac{2}{3}$ ounces)	560
Cream, 30 c.c. (1 ounce)	60
Lemon-juice, 30 c.c. (1 ounce)	12
Coffee, 150 c.c. (5 ounces)	00
Tea, 150 c.c. (5 ounces)	00
This furnishes seven feedings, 1 containing[2]:	
Coffee, 150 c.c. (5 ounces)	00
Egg, 1	75
Lactose, 30 grams (1 ounce)	120
Sugar, 5 grams	20
One feeding containing:	
Tea, 150 c.c. (5 ounces)	00
Cream, 30 c.c. (1 ounce)	60
Sugar, 5 grams	20

[1] Some of these combinations appeared in the Amer. Jour. Med. Sci., 1912, cxliii, 77; the others have been arranged by Miss Estelle Magill, Head Nurse of The Russell Sage Institute of Pathology.

[2] Beat the egg lightly in a cup; dissolve lactose thoroughly in very hot coffee; pour on to beaten egg (stir while pouring), strain, add sugar, and serve. This may be served hot or iced.

	Calories.
Four feedings, each containing:	
Milk, 200 c.c. (6⅔ ounces)	140
One feeding containing[1]:	
Egg, 1	75
Sugar, 15 grams (½ ounce)	60
Lemon-juice, 30 c.c. (1 ounce)	12
Water, 4 or 5 ounces	00
For 1500 calories a day:	
Milk, 1½ quarts (1500 c.c.)	1000
Cream, 1⅔ ounces	100
Lactose, 3⅓ ounces (100 grams)	400
This furnishes six feedings, each containing:	
Milk, 8 ounces	160
Cream, 2 drams	15
Lactose, 16 grams	64
Or	
Eggs, 2	150
Lactose, 110 grams (3¾ ounces)	440
Sugar, 25 grams (⅘ ounce)	100
Milk, 800 c.c. (26⅔ ounces)	560
Cream, 120 c.c. (4 ounces)	240
Lemon-juice, 30 c.c. (1 ounce)	00
Coffee, 150 c.c. (5 ounces)	00
Tea, 150 c.c. (5 ounces)	00
This furnishes one feeding containing:	
Coffee, 150 c.c. (5 ounces)	00
Egg, 1	75
Lactose, 40 grams (1⅓ ounces)	160
Sugar, 5 grams (⅙ ounce)	20
One feeding containing:	
Tea, 150 c.c. (5 ounces)	00
Cream, 50 c.c. (1⅔ ounces)	100
Lactose,[2] 30 grams (1 ounce)	120
Sugar, 5 grams	20
Four feedings, each containing:	
Milk, 200 c.c. (6⅔ ounces)	140
Cream, 17 c.c., large tablespoonful	34

[1] Dissolve sugar in water; add lemon-juice, and pour on to beaten egg; add cracked ice, strain, and serve. Or, dissolve sugar in water and put with other ingredients into a shaker; shake up thoroughly, strain, and serve.

[2] Lactose to be thoroughly dissolved in very hot tea before adding cream.

One feeding containing:	Calories.
Egg, 1	75
Lactose,[1] 40 grams (1⅓ ounces)	160
Sugar, 15 grams (½ ounce)	60
Lemon-juice, 30 c.c. (1 ounce)	12
Water, 4 or 5 ounces.	

For 2000 calories a day:

Milk, 1½ quarts	1000
Cream, 8 ounces (240 c.c.)	500
Lactose, 4 ounces (120 gm.)	500

This furnishes seven feedings, each containing:

Milk, 7 ounces	140
Cream, 1 ounce	60
Lactose, 18 grams	72

Or

Eggs, 2	150
Lactose, 125 grams (4 ounces)	500
Sugar, 15 grams (½ ounce)	60
Milk, 1000 c.c. (32 ounces)	700
Cream, 240 c.c. (8 ounces)	480
Cocoa, 5 grams	25
Orange-juice, 60 c.c. (2 ounces)	30
Lemon-juice	negligible 00
Coffee, 150 c.c. (5 ounces)	00

This furnishes one feeding containing:

Coffee, 150 c.c. (5 ounces)	00
Egg, 1	75
Lactose, 50 grams (1⅔ ounces)	200
Sugar, 5 grams	20

One feeding containing:

Cocoa, 5 grams	25
Milk, 120 c.c. (4 ounces)	80
Cream, 60 c.c. (2 ounces)	120
Lactose, 50 grams	200

One feeding containing:

Egg, 1	75
Lactose, 40 grams (1⅓ ounces)	160
Sugar, 10 grams	40
Orange-juice, 120 c.c. (4 ounces)	60
Lemon-juice, 1 to 2 teaspoonsful.	

Four feedings containing:

Milk, 210 c.c. (7 ounces)	140
Cream, 45 c.c. (1½ ounces)	90

[1] Boil lactose and sugar in water for two minutes and cool before adding lemon-juice.

For 2500 calories a day: Calories.

Milk, 1½ quarts 1000
Cream, 8 ounces 500
Lactose, 8 ounces (240 grams) 1000

This furnishes seven feedings, each containing:

Milk, 7 ounces 140
Cream, 1 ounce 60
Lactose, 36 grams 144

Or

Milk, 1000 c.c. 700
Cream, 240 c.c. (8 ounces) 480
Eggs, 3 225
Lactose, 165 grams (5½ ounces) 660
Sugar, 40 grams 160
Bread, 1 slice, 30 grams 80
Uneeda Biscuit, 1 25
Butter, 10 grams (⅓ ounce) 80
Orange-juice, 120 c.c. (4 ounces) 60
Lemon-juice (1½ ounces) 20

This furnishes one feeding containing:

Coffee, 150 c.c. (5 ounces) 00
Egg, 1 75
Lactose, 40 grams (1⅓ ounces) 160
Sugar, 5 grams 20
Toast, 1 slice 80
Butter, 10 grams 80

One feeding containing:

Egg, 1 75
Lactose, 50 grams (1⅔ ounces) 200
Orange-juice, 120 c.c. (4 ounces) 60
Sugar, 10 grams 40
Lemon-juice to taste.
Water.

One feeding containing:

Egg, 1 75
Milk, 200 c.c. (6⅔ ounces) 140
Cream, 40 c.c. (1⅓ ounces) 80
Lactose, 25 grams (⅝ ounce) 100
Sugar, 5 grams 20
Flavor with vanilla or nutmeg.

One feeding containing:

Lactose, 60 grams (2 ounces) 240
Sugar, 20 grams (⅔ ounce) 60
Lemon-juice, 30 or 40 c.c. (1 or 1⅓ ounces) 15

Four feedings, each containing:

Milk, 200 c.c. (6⅔ ounces) 140
Cream, 50 c.c. (1⅔ ounces) 100

For 3000 calories a day:	Calories.
Milk, 1½ quarts	1000
Cream, 1 pint (480 c.c.)	1000
Lactose, 8 ounces	1000
This furnishes eight feedings, each containing:	
Milk, 6 ounces	120
Cream, 2 ounces	120
Lactose, 1 ounce	120
Or	
Breakfast:	
Farina	100
Toast, 1 slice (30 grams before toasting)	80
Cream, 100 c.c. (3½ ounces)	200
Butter, 8 grams	60
Lactose, 40 grams (1⅓ ounces)	160
Sugar, 20 grams	80
Coffee, 1 large cup or 2 small cups (300 c.c.)	00
10–10.30 A. M.:	
Milk, 200 c.c. (6⅔ ounces)	140
Cream, 50 c.c. (1⅔ ounces)	100
Dinner:[1]	
Eggs, 2	150
Potato, 1 medium, about	100
Bread, 1 slice, or roll, 1, about	80
Butter, 30 grams (1 ounce)	234
Apple, 1 medium (pared and cored)	75
Sugar, 15 grams (½ ounce)	60
3 to 4 P. M.:	
Tea, 150–200 c.c.	—
Lactose, 50 grams	200
Sugar, 5 grams	20
Cream, 50 c.c. (1⅔ ounces)	100
Crackers, 3 Uneeda, or 2 soda, toasted	75
Butter, 8 grams	62
Supper:	
Rice, 25 grams, or farina, cooked with	100
Milk, 100 c.c. (3½ ounces)	70
Toast, 30 grams (1 slice)	80
Butter, 8 grams	62
Sugar, 5 grams (for cereal)	20
Cream, 60 c.c. (2 ounces)	120
Orange, 1 slice	100
Sugar, 5 grams (with orange)	20

[1] Potato baked, served with butter. Apple baked with 15 grams sugar and about 8 grams butter. Some patients will eat more butter if unsalted butter is used in the diet.

8 to 9 P. M.:	Calories.
Cocoa, 5 grams	25
Sugar, 10 grams	140
Milk, 150 c.c. (5 ounces)	105
Cream, 30 c.c. (1 ounce)	60
Lactose, 25 grams	100

For 3900 calories a day:

Milk, 1½ quarts	1000
Cream, 1 pint	1000
Lactose, 16 ounces (480 grams)	900

This furnishes eight feedings, each containing:

Milk, 6 ounces	120
Cream, 2 ounces	120
Lactose, 2 ounces	240

Further Details of Administration.—Further details of the administration of the diet will be illustrated by extracts from the histories of patients treated in the Metabolism Ward of the Russell Sage Institute of Pathology in affiliation with Second Medical Division of Bellevue Hospital.[1]

The patient whose dietary follows was under observation to determine the relative values of fat and carbohydrate as sparers of body protein. During alternate periods fat and carbohydrate preponderated in the diet:

DIET WHILE TEMPERATURE RANGED FROM 104°–100.6° F.

First Day:	*Fat Preponderating*	Calories.
6.30 A. M.:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 125 c.c. (4 ounces)	250
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 125 c.c. (4 ounces)	250
12 NOON:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 150 c.c. (5 ounces)	300
2.30 P. M.:	Lactose, 75 grams (2½ ounces)	300
	Sugar, 30 grams (1 ounce)	120
	Lemon-juice, 50 c.c. (1⅔ ounces)	20
5.00 P. M.:	Eggs, 2½	190
	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 250 c.c. (8 ounces)	500

[1] All of the dietaries which follow were arranged and administered under the supervision of Miss Magill.

First Day:	*Fat Preponderating*	Calories.
7.30 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 150 c.c. (5 ounces)	300
9.30 P. M.:	Lactose, 65 grams (2 ounces)	260
	Sugar, 18 grams	72
	Lemon-juice, 40 c.c. (1⅓ ounces)	15
12 MIDNIGHT:	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 200 c.c.	400
		4000
Second Day:		
6.00 A. M.:	Eggs, 2	150
	Milk, 150 c.c. (5 ounces)	105
	Lactose, 50 grams (1⅔ ounces)	200
	Bread, 35 grams (1 slice), toasted	95
	Butter, 20 grams (⅔ ounce)	156
	Coffee, 200 c.c. (6⅔ ounces)	—
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
12 NOON:	Eggs, 2	150
	Milk, 50 c.c. (1⅔ ounces)	35
	Lactose, 30 grams (1 ounce)	120
	Butter, 18 grams (⅔ ounce)	140
	Tea, 200 c.c. (6⅔ ounces)	—
3.00 P. M.:	Egg,[1] 1	150
	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 200 c.c. (6⅔ ounces)	400
	Sugar, 10 grams	40
5.30 P. M.:	Egg yolks,[2] 4 large, about 75 grams	279
	Egg whites, 3 large, about 96 grams	48
	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 250 c.c. (8⅓ ounces)	500
8.00 P. M.:	Lactose, 50 grams (1⅔ ounces)	200
	Sugar, 30 grams (1 ounce)	120
	Lemon-juice, 40 c.c. (1⅓ ounces)	15
12 MIDNIGHT:	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 250 c.c. (8⅓ ounces)	500
		3680
Third Day:		
6.00 A. M.:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 100 c.c. (3⅓ ounces)	200
	Cream (heavy), 50 c.c. (1⅔ ounces)	170
	Coffee, 200 c.c.	—
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 125 c.c. (4 ounces)	250

[1] Made into egg-nog.

[2] Eggs coddled in cup; drank milk and cream mixed.

Third Day:	*Fat Preponderating*	Calories.
12 NOON:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 150 c.c. (5 ounces)	300
	Butter, 10 grams	78
3.00 P. M.:	Cream, 275 c.c. (9 ounces)	550
5.00 P. M.:	Eggs, 2	150
	Cream, 250 c.c. (8 ounces)	500
	Butter, 10 grams	78
8.00 P. M.:	Cream, 250 c.c. (8 ounces)	500
12 MIDNIGHT:	Cream, 250 c.c. (8 ounces)	500
		4000
First Day:	*Carbohydrate Preponderating*	
6.00 A. M.:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Lactose, 50 grams (1⅔ ounces)	200
	Butter, 6 grams	47
	Crackers, 18 grams (2 soda crackers)	72
9.30 A. M.:	Milk, 300 c.c.	210
	Crackers, 18 grams (2 soda crackers)	72
12 NOON:	Eggs, 2	150
	Milk, 100 c.c. (3⅓ ounces)	70
	Lactose, 60 grams (2 ounces)	240
	Butter, 15 grams (½ ounce)	117
	Crackers, 27 grams (3 soda crackers)	108
3.00 P. M.:	Egg, 1	75
	Milk, 200 c.c. (6⅔ ounces)	140
	Sugar, 5 grams	20
5.30 P. M.:	Lactose, 110 grams	440
	Sugar, 40 grams (1⅓ ounces)	160
	Lemon-juice, 75 c.c.	30
	Crackers, 18 grams (2 soda crackers)	72
7.30 P. M.:	Milk, 375 c.c. (12½ ounces)	260
	Crackers, 9 grams (1 soda cracker)	36
9.30 P. M.:	Milk, 225 c.c. (7½ ounces)	158
	Cream, 125 c.c.	250
12 MIDNIGHT:	Egg, 1	75
	Lactose, 60 grams	240
	Lemon-juice, 50 c.c. (1⅔ ounces)	20
	Sugar, 25 grams	100
		3666
Second Day:		
6.00 A. M.:	Eggs, 2	150
	Milk, 200 c.c.	140
	Lactose, 50 grams (1⅔ ounces)	200
	Butter, 6 grams	47
	Crackers, 18 grams	72
9.30 A. M.:	Milk, 350 c.c.	245

Second Day:	*Carbohydrate Preponderating*	Calories
12 NOON:	Eggs, 2	150
	Lactose, 150 grams	600
	Lemon-juice, 75 c.c.	30
	Crackers, 30 grams	120
	Butter, 10 grams	78
2.30 P. M.:	Milk, 350 c.c.	245
	Crackers, 18 grams	72
	Butter, 4 grams	31
5.30 P. M.:	Eggs, 2	150
	Milk, 300 c.c.	210
	Lactose, 30 grams	120
	Butter, 14 grams	109
8.00 P. M.:	Milk, 200 c.c.	140
12 MIDNIGHT:	Egg, 1	75
	Lactose, 50 grams	200
	Crackers, 7 grams	28
	Lemon-juice, 25 c.c.	10
		3222

Control of Diarrhea by Increase of Fat.—The following patient entered the ward suffering from active diarrhea; he complained also of nausea. In this instance the diarrhea was controlled by decreasing the carbohydrate and increasing the amount of fat in the diet. The patient is exceptional in the amount of fat tolerated.

TEMPERATURE RANGING FROM 104°–102° F.

One-third of Non-protein Calories Furnished by Fat, Two-thirds by Carbohydrate.

First Day:		Calories.
7.00 A. M.:	Milk, 375 c.c. (13½ ounces)	263
	Lactose, 25 grams	100
	Bread, 42 grams (1 large slice)	113
	Butter, 5 grams	40
	Sugar, 10 grams	40
	Coffee, 100 c.c. (strong)	—
9.30 A. M.	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 70 c.c. (2⅓ ounces)	140
	Lactose, 15 grams (½ ounce)	60
	Cracker, 8 grams (1 soda cracker)	32
12 NOON:	Egg,[1] 1	75
	Milk, 175 c.c. (6 ounces)	128
	Lactose, 25 grams	100
	Farina, 20 grams	74

[1] Egg and lactose stirred into cooked farina, served with milk.

First Day:		Calories.
2.30 P. M.:	Egg white,[1] 1	15
	Milk, 200 c.c.	140
	Lactose, 15 grams	60
5.30 P. M.:	Milk, 150 c.c. (5 ounces)	105
	Cream, 25 c.c.	50
	Lactose, 15 grams (½ ounce)	60
	Bread, 33 grams (1 slice)	80
9.00 P. M.:	Milk, 125 c.c.	108
	Lactose, 50 grams	200
	Cracker, 8 grams	32
	Tea, 200 c.c.	—
12.30 A. M.:	Milk, 350 c.c.	245
3.30 A. M.:	Egg white, 1 large	18
	Lactose, 60 grams	240
	Sugar, 15 grams	60
	Lemon-juice, 50 c.c.	20
		2750

There were nine defecations this day.

Two-thirds of Non-protein Calories Furnished by Fat, One-third by Carbohydrate.

Second Day:		Calories.
6.30 A. M.:	Milk, 350 c.c. (11⅔ ounces)	245
	Cream, 50 c.c. (1⅔ ounces)	100
	Lactose, 35 grams	140
	Sugar, 10 grams	40
	Bread, 41 grams (1 large slice), toasted	110
	Butter, 8 grams	62
	Coffee, 200 c.c.	—
9.30 A. M.	Milk, 250 c.c.	175
	Sugar, 15 grams (½ ounce), gruel	60
	Arrowroot, 4 grams	15
1.00 P. M.	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 150 c.c. (5 ounces)	300
	Bread, 40 grams (1 large slice)	108
	Butter, 10 grams	78
2.40 P. M.	Egg white,[2] 1	15
	Milk, 150 c.c. (5 ounces)	105
	Cream, 50 c.c. (1⅔ ounces)	100
	Rice, 15 grams (½ ounce)	57

[1] Egg white beaten into warm milk in which lactose was dissolved; nutmeg flavoring.

[2] Rice cooked with small amount of water and 150 c.c. milk. Egg white beaten into hot rice mixture; served with cream.

Second Day:		Calories.
5.30 P. M.:	Egg,[1] 1	75
	Milk, 100 c.c.	70
	Cream, 80 c.c.	160
	Sugar, 5 grams	20
8.30 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 100 c.c. (3½ ounces)	200
12.30 A. M.:	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 100 c.c. (3½ ounces)	200
3.30 A. M.:	Egg, 1	75
	Milk, 100 c.c. (3½ ounces)	70
	Cream, 100 c.c. (3½ ounces)	200
	Sugar, 5 grams	20
		3000

There were eight defecations this day.

Three-quarters of Non-protein Calories Furnished by Fat, One-quarter by Carbohydrate.

Third Day:		Calories.
6.30 A. M.:	Milk, 150 c.c. (5 ounces)	105
	Cream, 150 c.c. (5 ounces)	300
	Bread, 42 grams (1 large slice), toasted	115
	Butter, 15 grams	117
	Sugar, 5 grams	20
	Coffee, 150 grams c.c.	—
9.30 A. M.:	Milk, 150 c.c.	105
	Cream, 100 c.c.	200
	Arrowroot, 8 grams, gruel	30
	Sugar, 5 grams	20
	Cracker, 9 grams, (1 soda cracker)	36
	Butter, 3 grams	23
12 NOON:	Egg, 1	75
	Milk, 50 c.c.	37
	Cream, 100 c.c.	200
	Bread, 30 grams	80
	Butter, 6 grams	47
2.30 P. M.:	Ice cream, 100 grams	100
	Cream, 50 c.c. (1⅔ ounces)	100
6.00 P. M.:	Egg,[2] 1	75
	Milk, 120 c.c.	84
	Cream, 150 c.c.	300
	Sugar, 5 grams	20
	Farina, 10 grams	40
8.30 P. M.:	Milk, 150 c.c.	105
	Cream, 150 c.c.	300

[1] Milk and cream mixed, heated, and sugar added; beat in egg while hot, to lightly cook egg, but not thicken.

[2] Soft custard made of egg, milk, and part of cream.

Third day:		Calories.
12.30 A. M.:	Egg, 1	75
	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 100 c.c. (3⅓ ounces)	200
		3000

There were three defecations this day.

Fat furnished 2500 Calories; Carbohydrate, 200 Calories.

Fourth Day:		Calories.
6.30 A. M.:	Eggs, 2½ (scrambled)	190
	Cream, 200 c.c. (6⅔ ounces)	400
	Coffee, 200 c.c. (6⅔ ounces)	—
10.00 A. M.:	Egg, 1 (very large)	90
	Cream, 150 c.c. (5 ounces)	300
12.30 P. M.:	Eggs,[1] 3	225
	Cream, 100 c.c. (3⅓ ounces)	200
	Tea, 200 c.c. (6⅔ ounces)	—
2.40 P. M.:	Egg, 1	75
	Cream, 100 c.c. (3⅓ ounces)	200
5.30 P. M.:	Eggs,[2] 2½ (scrambled)	190
	Cream, 150 c.c. (5 ounces)	300
	Tea, 200 c.c. (6⅔ ounces)	—
8.30 P. M.:	Egg[3] white, 1	15
	Yolks, 2½	150
	Cream, 150 c.c. (5 ounces)	300
12.30 A. M.:	Egg white, 1	15
	Yolks, 2	120
	Cream, 150 c.c. (5 ounces)	300
		3070

There was one defecation on this day. This diet was given for four consecutive days. An attempt was then made to change to high carbohydrate with low fat, with the result that patient vomited several feedings and had two defecations: When fat was added to diet patient retained all nourishment.

Patient with Intestinal Hemorrhage.—This patient suffered from intestinal hemorrhage. *The food was stopped immediately.* But since feeding must be resumed after a hemorrhage, the diet charts of the patient are given to illustrate the procedure in this instance. As the hemorrhage appeared to have ceased, food was given tentatively the day following, *the nurse having strict*

[1] Eggs coddled in cup; cream put in tea.

[2] Part of cream mixed with eggs for scrambling.

[3] About 2 ounces of water added to cream which was heated; eggs beaten and stirred into hot fluid; sweetened with saccharin, flavored with nutmeg.

orders to stop it should signs of bleeding recur. The moderate hemorrhage on this day did not seem to contraindicate the continuance of the food, and the event justified the opinion.

DAY BEFORE HEMORRHAGE

		Calories.
6 A. M.:	Milk, 250 c.c. (8½ ounces)	175
	Cream, 50 c.c. (1⅔ ounces)	100
9.30 A. M.:	Milk, 150 c.c. (5 ounces)	105
	Cream, 50 c.c. (1⅔ ounces)	100
12 NOON:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 25 c.c. (⅝ ounce)	50
2.30 P. M.:	Ice cream, 112 grams (3⅔ ounces)	112
5.30 P. M.:	Milk, 250 c.c. (8 ounces)	175
	Cream, 50 c.c. (1⅔ ounces)	100
8.00 P. M.:	Egg, 1⅓	100
	Milk, 150 c.c. (5 ounces)	105
	Cream, 100 c.c. (3⅓ ounces)	200
	Sugar, 10 grams	40
	Nutmeg for flavoring.	

DAY OF HEMORRHAGE

First appearance of hemorrhage 5 A. M. next morning. No food given during day. Patient drank large amount of water and complained of hunger in the afternoon.

FOLLOWING DAY—MODERATE HEMORRHAGE

10 A. M.:	Eggs, 2	150
	Bread, 54 grams (toasted)	146
	Butter, 13 grams	100
	Cream, 50 c.c. (1⅔ ounces)	100
	Sugar, 10 grams	40
	Coffee, 200 c.c. (6⅔ ounces)	—
12.30 P. M.:	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 35 c.c.	70
	Bread, 1 slice, 32 grams	86
	Butter, 3 grams	23
2.30 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
5 P. M.:	Milk, 250 c.c. (8 ounces)	175
	Cream, 50 c.c. (1⅔ ounces)	100
8 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 100 c.c. (3⅓ ounces)	200
	Milk, 200 c.c. (6⅔ ounces)	140
12 MIDNIGHT:	Cream, 100 c.c. (3⅓ ounces)	200
	In twenty-four hours	1880

Next day slight hemorrhage; one stool. Morning of the fourth day after patient had formed, normal defecation.

Diet During the First Week of Convalescence.—The patient was a twelve-year-old boy. His weight was 36 kilograms. Convalescence was dated from the first day the temperature remained below 100° F.

First Day:		Calories.
7 A. M.:	Eggs, 2	150
	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 50 c.c. (1⅔ ounces)	100
	Coffee, 100 c.c.	—
	Sugar, 10 grams	40
	Bread, 24 grams (small slice toast)	65
	Butter, 6 grams	47
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 100 c.c. (3⅓ ounces)	200
12 NOON:	Bread, 42 grams (1½ slices)	113
	Butter, 22 grams	172
	Roast turkey, 18 grams	60
	Potato, 125 grams, mashed with	113
	Cream, 50 c.c.	100
	Ice cream, 100 grams (3½ ounces), about	200
	Orange, 75 grams (2½ ounces)	38
5.30 P. M.:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Lactose, 25 grams (⅞ ounce)	100
	Sugar, 10 grams	40
	Cocoa, 5 grams	25
	Bread, 40 grams (large slice)	108
	Butter, 12 grams	94
8 P. M.:	Orange (sliced), 75 grams (2½ ounces)	38
	Sugar, 10 grams	40
		2343
Second Day:		
7 A. M.:	Eggs, 2	150
	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 50 c.c. (1⅔ ounces)	100
	Coffee, 100 c.c.	—
	Sugar, 10 grams	40
	Bread, 24 grams (small slice toast)	65
	Butter, 6 grams	47
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 50 c.c. (1⅔ ounces)	100
12 NOON:	Eggs, 2	150
	Potato, 80 grams (2⅔ ounces)	72
	Bread, 114 grams (3½ slices)	308
	Butter, 30 grams (1 ounce)	234
	Milk, 200 c.c. (6⅔ ounces)	140

		Calories.
Second Day:		
12 NOON:	Cream, 100 c.c. (3½ ounces)	200
	Lactose, 25 grams	100
	Sugar, 10 grams	40
	Cocoa, 5 grams	25
2.30 P. M.:	Ice cream, 118 grams	118
5.30 P. M.:	Egg, 1	75
	Milk, 250 c.c. (8 ounces)	175
	Bread, 12 grams	32
	Butter, 2 grams	16
8 P. M.:	Rice, 15 grams (½ ounce)	57
	Milk, 300 c.c. (10 ounces)	210
	Cream, 50 c.c. (1⅔ ounces)	100
	Sugar, 10 grams	40
		2804
Third Day:		
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
11.30 A. M.:	Eggs, 2	150
	Potato, 100 grams (3½ ounces)	90
	Bread, 117 grams (3½ slices)	316
	Butter, 25 grams (⅞ ounce)	195
	Cream, 100 c.c.	200
	Lactose, 25 grams	100
	Sugar, 10 grams	40
	Tea, 200 c.c. (6⅔ ounces)	—
2.30 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 50 c.c. (1⅔ ounces)	100
	Sugar, 10 grams	40
	Cocoa, 5 grams	25
5.30 P. M.:	Eggs,[1] 2	150
	Milk, 150 c.c. (5 ounces)	105
	Cream, 125 c.c. (4 ounces)	250
	Sugar, 15 grams	60
	Dried apples,[2] 20 grams (⅔ ounce)	56
	Bread, 23 grams (small slice)	62
	Butter, 12 grams	94
8.30 P. M.:	Cream, 100 c.c. (3½ ounces)	200
	Milk, 200 c.c. (6⅔ ounces)	140
		2653
Fourth Day:		
6.30 A. M.:	Eggs, 2	150
	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 25 c.c.	50
	Oatmeal, 10 grams	40
	Bread, 68 grams (2 slices toast)	184

[1] Small amount of cream cooked with scrambled eggs.

[2] Dried apples made into apple sauce.

Fourth Day:		Calories.
6.30 A. M.:	Butter, 20 grams (⅔ ounce)	156
	Lactose,[1] 25 grams	100
	Sugar, 5 grams	20
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
12 NOON:	Eggs, 2	150
	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 50 c.c. (1⅔ ounces)	100
	Potato,[2] 112 grams (3⅔ ounces)	100
	Bread, 106 grams (about 3 slices)	286
	Butter, 20 grams (⅔ ounce)	156
	Sugar, 10 grams	40
	Tea, 200 c.c.	—
2.30 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Lactose, 25 grams	100
	Sugar, 10 grams	40
	Cocoa, 5 grams	25
5.30 P. M.:	Egg, 1	75
	Milk, 225 c.c. (7½ ounces)	158
	Cream, 35 c.c. (1⅙ ounces)	70
	Bread, 20 grams (⅔ ounce)	54
	Butter, 10 grams	78
	Sugar,[3] 2 grams	8
	Arrowroot, 2 grams	8
8.00 P. M.:	Milk, 200 c.c. (6⅔ ounces)	140
	Cream, 100 c.c. (3⅓ ounces)	200
		2943
Fifth Day:		
6.30 A. M.:	Eggs, 2	150
	Milk, 150 c.c. (5 ounces)	105
	Cream, 50 c.c. (1⅔ ounces)	100
	Oatmeal, 25 grams	100
	Bread, 111 grams (3⅓ slices)	300
	Butter, 23 grams	179
	Lactose, 25 grams	100
	Coffee, 150 c.c. (5 ounces)	—
	Sugar, 5 grams	20
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
12 NOON:	Eggs, 2	150
	Cream, 100 c.c. (3⅓ ounces)	200
	Potato,[4] 100 grams (3⅓ ounces)	90
	Bread, 109 grams (3⅓ slices)	294
	Butter, 16 grams (½ ounce)	125

[1] Given in milk to drink.

[2] Potato mashed, using part of milk and cream, balance of which was put in tea.

[3] Cooked with part of milk.

[4] Creamed potatoes using half of cream; balance put in tea.

Fifth Day:		Calories.
12 NOON:	Lactose, 25 grams	100
	Sugar, 5 grams	20
	Tea, 200 c.c.	—
2.30 P. M.:	Ice cream, 100 grams (3½ ounces)	100
5.30 P. M.:	Eggs, 2	150
	Milk, 50 c.c. (1⅔ ounces)	35
	Cream, 75 c.c. (2½ ounces)	150
5.30 P. M.:	Tapioca,[1] 10 grams	37
	Sugar, 20 grams (⅔ ounce)	80
	Bread, 126 grams (about 4 slices)	340
	Butter, 20 grams (⅔ ounce)	156
	Tea, 200 c.c.	—
8.30 P. M.:	Cream, 100 c.c.	200
	Milk, 200 c.c.	140
	Soda crackers, 18 grams, 2 crackers	76
	Lactose, 25 grams	100
	Sugar, 10 grams	40
		3777
Sixth Day:		
6.30 A. M.:	Eggs, 2	150
	Milk, 150 c.c. (5 ounces)	105
	Lactose, 25 grams	100
	Sugar, 10 grams	40
	Bread, 108 grams (about 3⅓ slices)	291
	Butter, 20 grams (⅔ ounce)	156
	Oatmeal, 25 grams	100
9.30 A. M.:	Milk, 200 c.c. (6⅔ ounces)	140
12 NOON:	Eggs, 2	150
	Milk, 100 c.c. (3⅓ ounces)	70
	Cream, 25 c.c.	50
	Potato, 100 grams (3½ ounces)	90
	Bread, 145 grams (about 4½ slices)	392
	Butter, 15 grams (½ ounce)	117
	Lactose, 25 grams	100
	Tea, 200 c.c. (6⅔ ounces)	—
2.30 P. M.:	Ice cream, 100 grams	100
5.30 P. M.:	Eggs, 2	150
	Milk, 275 c.c. (9 ounces)	193
	Cream, 50 c.c. (1⅔ ounces)	100
	Lactose, 25 grams	100
	Sugar, 5 grams	20
	Bread, 109 grams (about 3⅓ slices)	294
	Butter, 18 grams	140
	Tea, 200 c.c.	—
	Lactose, 25 grams	100

[1] Tapioca pudding; part of sugar and cream was eaten with pudding.

Sixth Day:		Calories.
8.00 P. M.:	Milk, 200 c.c.	140
	Sugar, 10 grams	40
	Cocoa, 5 grams	25
	Soda crackers, 18 grams, 2 crackers	76
		3529

Beneficial Effects of High Calory Diet.—It was pointed out early in the study of the high calory diet that its value would ultimately be decided by the results obtained from its use. This is the final test of every therapeutic procedure. Judged by this standard, the advocacy of the diet has been amply justified. During ten years no opportunity has been lost to study its effects upon the individual patient or upon groups of patients. It has been shown that typhoid patients have remarkably good digestions; that they absorb foods, even in large amounts, about as well as healthy men; and that they consume, or lay by, the food they absorb under the laws which govern the nutritive processes in health.

The benefit to the individual patient from maintaining him in the best possible state of nutrition became apparent early in the study of the diet. The influence of the diet upon the natural history of typhoid fever has only recently been demonstrated through a statistical study of some 450 patients, half of them on the high calory diet, and half of them on diets furnishing not more than 1000 to 1500 calories a day.

The most striking fact brought out by this study is that certain symptoms of the disease, which hitherto have been attributed to the specific action of the typhoid bacillus, are due to faulty methods of treatment, in particular, to an inadequate or improperly balanced diet. Severe nervous disturbances do not occur in patients who are well nourished. They lose but little weight. They take a lively interest in what is going on about them. Many of them feed themselves from trays placed on or near the bed.

There is no evidence that the duration or height of the initial febrile movement is affected by diet except, perhaps, that long recrudescences are rarer. The total duration of the disease,

however, is shortened, in some instances by months, through the shortening of convalescence.

Tympanites and diarrhea occur much less frequently. When they occur, they are due to faulty arrangement of the diet except in rare instances.

Intestinal hemorrhage is not less frequent, but the mortality in cases with hemorrhage has been reduced from approximately 30 to 10 per cent. Perforation occurred only twice in the high calory group (0.9 per cent.), and seven times in the milk series (3.15 per cent.). One of the high calory cases with perforation died, 6 of the 7 milk cases died.

With the statistics uncorrected, the mortality from typhoid fever has been reduced from 17.6 to 8.10 per cent. by the high calory diet. If the statistics be corrected for patients who refused or were unable to take their food, or who had complicating conditions (diphtheria, status lymphaticus, alcoholism), the mortality of the high calory groups falls to 4.50 per cent.

In conclusion, the author believes that the principle underlying the high calory diet is applicable to other febrile diseases than typhoid fever. In practice he employs the diet, in more or less modified form, in all fevers, unless there is some definite contraindication to the procedure.

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THE TREATMENT OF LOBAR PNEUMONIA

The Importance of Determining the Etiologic Agent in Each Case of Pneumonia and Full Discussion of the Various Methods of Treatment; the Use of Digitalis in the Early Stages.

With the exception of facial erysipelas there probably is no infectious disease for which more vaunted forms of treatment and so-called cures have been proposed than for pneumonia. Probably without exception there is no infectious disease for which treatment has accomplished less than pneumonia. The amount of harm that has been done by treatment in this disease is difficult to estimate, but is not inconsiderable.

Certain of the methods of treatment have had a short-lived day; others have clung with surprising tenacity, and only after reappearing again and again have they finally been consigned to oblivion. Venesection is not the only one of these curative measures that have had a cat-like life. Their name is legion. The reason for this is that first impressions are lasting ones, and recovery from pneumonia is not infrequently such a striking and dramatic episode that it is not surprising that when such an event follows on the heels of a new or untried measure, this measure is given the credit, and forever afterward in the observer's mind possesses curative value.

To disprove the value of a given therapeutic measure is more difficult than to establish the value of another. Most of the measures suggested have been susceptible to proof or disproof only with the most careful painstaking effort and observation.

Opportunities for such control have been difficult to obtain. As a result, the treatment commonly employed has been the result of argument and refutation, not the result of controlled observation and trial. It is, therefore, difficult to discuss the treatment of pneumonia in an unbiassed and truly scientific spirit. Shall we attack and omit in our treatment all that has not been proved of value, or shall we accept all that has been recommended by men of judgment and acumen? With most diseases neither method is the one to be employed exclusively. With pneumonia many of the methods proposed have not even a theoretic basis, and failure to use them is not likely to lay the physician open to the charge of malpractice by any jury of his fellows, or cause him to have a troubled conscience.

On the other hand, knowledge of this disease has been increasing, the various phenomena comprising the disease are being subjected to critical scientific analysis, and the physician is now in a position to employ at least a few measures which are based on a critical study. For these reasons the average physician will probably do best to rely on these few measures, and to employ, in addition, only those simple ones which are supported by common sense and have been shown to do no harm.

The treatment of pneumonia must commence with the diagnosis. Acute lobar pneumonia is the easiest of the acute infectious diseases to diagnose correctly. This is true, however, in the very earliest stages of the disease, only in those cases in which the onset is sudden, with chill, pain in the chest, etc. In a considerable number of cases the onset is gradual, with a number of days or even weeks of coryza or mild bronchitis preceding the actual onset of the pneumonia. This is why all cases with such symptoms should be carefully watched and any exacerbation of symptoms should at once raise the question of the possible onset of pneumonia. In the diagnosis of lobar pneumonia, physical examination is of the greatest importance, though in not an inconsiderable number of cases the diagnosis can be made at least with great probability even before the signs in the chest are outspoken or definite. In most cases, however, careful physical examination of the chest reveals signs

of consolidation, though often in a very small area, very early in the disease. It is often surprising within what a short time actual consolidation can occur. Even within twelve hours of the initial chill, preceding which the patient was feeling perfectly well, I have found well-marked and definite signs of pulmonary consolidation. In the absence of specific methods of treatment extremely early diagnosis was not of paramount importance. Since, however, we now possess a specific serum for the treatment of at least a portion of the cases of pneumonia, the question of early diagnosis is of great significance.

It is important, moreover, not only that the diagnosis of pneumonia be made, but that the etiologic agent in each case of pneumonia be determined.

I may recall to your mind that it has now been shown that there are at least four great groups of pneumococci which have been numbered I, II, III, and IV. These different varieties of pneumococci differ for the most part only in their immunologic reactions. So far no cultural differences between them have been detected. Now serum treatment has been demonstrated to be of value only in the cases due to pneumococci of Type I. These cases comprise about one-third of all the cases of pneumonia. If the serum treatment is applied indiscriminately to all cases it is evident that two-thirds of the cases would receive large doses of serum without any benefit. The detection of Type I cases, therefore, is of importance and, moreover, the detection should be made early, since the value of the serum depends largely upon the time at which it is administered, the earlier in the disease, the better. To make an etiologic diagnosis requires laboratory facilities, and the laboratory methods employed have been described elsewhere, so I shall not go into this matter here. In order that the laboratory manipulations may be carried out with success, however, it is very important that a specimen of sputum be obtained early in the disease, and that care be taken that this sputum be coughed up from the lung, and not simply consist of saliva which the patient has expectorated. The diagnosis of the condition and the obtaining of a suitable specimen of sputum are, therefore, the first two steps in the treat-

ment of pneumonia, at least so far as specific treatment is concerned.

The decision should then be made as to whether the patient shall be treated at home or in the hospital. If the patient is to be moved to a hospital, it is very important that this take place as early in the disease as possible. Most patients can undoubtedly be better cared for in a hospital, where there are facilities for moving the patient into the open air, than they can be in the average home. If patients are moved early in the disease it is not likely that transportation over short distances has much influence on the course of the disease, provided care be taken not to subject the patient to great exertion. A patient with lobar pneumonia should never be allowed to sit up or to dress himself, much less to walk to a chair or to the ambulance.

If the patient is to be treated at home, a room should be chosen which can be well ventilated by opening the windows from the top and bottom or, better, by complete removal of the windows. If possible, two rooms should be available, one of which can be kept warm, and arrangements be made so that the patient can be wheeled from one to the other. It is very important to make all these preparations early in the course of the disease, so that the patient may not be disturbed by moving or transportation, even to another part of the house, during the progress of the disease.

In order that the patient may later be treated with serum, provided the determination of the type of infection shows that this is advisable, efforts should be made to determine as quickly as possible whether or not the patient is sensitive to horse-serum, and also to desensitize him if he have even slight grades of sensitiveness, since it is well known that in highly sensitive patients the administration of horse-serum may give rise to alarming, even to serious symptoms. Fortunately, such reactions are rare. They are seen with small doses of serum as well as with large ones, and the rarity of such reactions is made evident by the fact that many physicians with very large experience in the treatment of diphtheria with antitoxic serum have never seen a severe or fatal reaction. Nevertheless, the physician is not

justified in permitting a patient to take risks which can be avoided. Precautions should be taken in the administration of sera of all kinds, but they are of special importance when anti-pneumococcic serum is to be administered, since in order to be effective this serum must be given in very large amounts, and intravenously. In order to detect whether the patient is sensitive to horse-serum or not, a very small amount—0.02 c.c. of horse-serum, diluted in salt solution 1 : 10, making the amount of horse-serum 0.002 c.c.—is injected intracutaneously (not under the skin) of the forearm. As a control, on the same level of the forearm is injected a similar amount of salt solution. In both cases, if the injections have been made correctly, slight wheals are seen, showing the depressions of the hair-follicles. These wheals disappear in a very few minutes as the fluid diffuses into the surrounding tissues. If the patient be sensitive, within an hour there appears at the site of injection of the horse-serum a definite urticarial wheal surrounded by an area of erythema. The size of the wheal and of the erythematous area is roughly proportional to the degree of sensitiveness which the patient possesses. If these signs do not appear within an hour, it is very good evidence that the patient is not highly sensitive to horse-serum, but is not conclusive proof that some reaction may not occur when large doses of serum are later administered. It has been shown, however, that even sensitive patients may be rendered insusceptible to the injection of large amounts of horse-serum by the previous injections of very small amounts which are insufficient to produce symptoms. Indeed, it has been shown that serum may be safely injected into highly sensitive animals provided the injections be made slowly enough. It is a very good rule, therefore, that about an hour following the intracutaneous test an injection of 0.5 to 1 c.c. of horse-serum be made subcutaneously. This is usually sufficient to desensitize the patient if intravenous injections of serum are to be made within the next twenty-four hours. Errors have been made by some writers on this subject in looking upon this subcutaneous injection as a test for sensitiveness. This subcutaneous injection is not a test injection, but is for the purpose of desensitization.

Such subcutaneous injections rarely give rise to local phenomena, and the only evidence such an injection would give of sensitiveness would be a general anaphylactic reaction.

If the intracutaneous test has shown the patient to be sensitive to horse-serum, more complex and elaborate efforts must be made to desensitize him, but it is inadvisable to carry these out until it has been determined whether or not serum is to be administered. I think it advisable, however, in order to save time that in every case of pneumonia, as soon as the clinical diagnosis is made, the intracutaneous tests, followed in an hour by the subcutaneous injection of 0.5 c.c. of serum be carried out as I have described. Usually within eight or ten hours the diagnosis of the type of infecting organism can be made by the laboratory methods to which we have previously referred. If such tests show that the patient is suffering from infection due to organisms other than pneumococci of Type I, no form of specific treatment should be attempted. If, however, the case is found to be due to pneumococci of this type, serum treatment should be immediately begun.

Other general methods of treatment should not be neglected, however, and in the cases due to infection with organisms other than Type I pneumococci we must rely entirely upon these more general and non-specific methods.

The diet in pneumonia is not of great importance, provided care be taken to avoid foods that may not be readily digested, and may give rise to gastro-intestinal symptoms. The most simple foods are usually all that are desired by the patient and all that he should have. It is well to see that the food contains sufficient nutritive value. The course of the disease being short, the importance of high caloric feeding to prevent waste is not so important as it is in typhoid. If patients will not take milk, custards, etc., in sufficient amounts to provide them with a fairly liberal allowance of energy-producing substances, recourse may be had to the administration of carbohydrates, in the form of milk-sugar, as is now so widely practised in the treatment of typhoid fever. The fluids taken by the patient should be carefully measured, and should amount to at least 3000 c.c. each day.

Many of the older physicians employed active purgatives at the onset of pneumonia, just as was done at the onset of the other acute infectious diseases. In our opinion there is little to be gained by active purgation in this disease. It is important that the bowels move regularly every day, either by the use of mild laxatives or, better, by an enema every morning, but in the absence of intestinal symptoms, care should be taken to prevent bringing them on by the administration of purgatives.

In most cases of pneumonia during the early days of the disease little or no drug treatment is required. It is our practice, however, to commence the administration of digitalis very early. The purpose of this early administration is not to produce immediate effects upon the heart, but to put the patient into such a condition that later if need arises physiologic digitalis effects may quickly be obtained by the administration of small doses by mouth. For this purpose we have found that 1 gram of digipuratum, given over a period of two days, is sufficient, and at the end of this time, unless there are signs of cardiac insufficiency, the administration of this drug should be discontinued. Instead of digipuratum, other preparations of digitalis may be employed in corresponding doses, but we have employed this drug because of its accurate standardization and ease of administration.

The chief symptoms from which the patient suffers during the earlier stages of pneumonia are pain in the chest and cough. The efforts on the part of physicians to relieve the chest pain have led to the employment of a great variety of measures, both local and general. After a considerable experience in the treatment of pneumonia, I have never been able to convince myself that any local measure can be relied upon to give relief in all cases. In certain instances the use of the old-fashioned flaxseed poultice has seemed to be accompanied by some relief of the pain. In the greater number of instances I think the use of a large ice-bag, if persisted in until the skin becomes thoroughly refrigerated, has more often been of relief. It is questionable, however, whether either of these measures is worth the effort and whether attempts to persuade the patient to employ them for a longer

time, in case results are not very quickly obtained, are justifiable. Where the cough and pain are very severe and troublesome most relief is probably obtained by the use of small doses of morphin, given subcutaneously and repeated frequently enough to dull the patient's sensibilities. I have failed to see any bad effects of the use of morphin in these cases unless it has been employed in very large amounts. In many cases of pneumonia morphin is undoubtedly of value, not only as a means of relief from pain, but in quieting the patient and preventing the undue expenditure of energy.

Local applications having for their purpose a modification of the local inflammatory process have been used from time immemorial. Many able physicians think the application of dry cups is of value. It is very unwise to be dogmatic about this. I can only say that in my experience I have never seen cupping to be of benefit, and the explanation of the supposed effectiveness of this form of treatment seems to me to be far fetched and inconclusive. The same may be said for the application of poultices and ice to the chest. The slight redistribution of blood and fluid in the neighborhood of the lesion by such methods can have very little effect upon the course of the inflammatory process within the chest. The majority of our patients are treated without any such local applications. I think it is well to have soft padded jackets which patients suffering from pneumonia can wear. These keep the chest warm and are very comfortable and grateful to the patients. They should be open at the sides and tied with tapes, so that examination of the chest can be made without causing the patient to make too great effort during the removal of the coverings.

The employment of hydrotherapy in pneumonia is a question about which there has been much discussion. It is probable that in most hospitals at present some form of hydrotherapy is employed. In most cases the use of tub baths, which was at one time warmly recommended by certain physicians, has been almost entirely given up. Where hydrotherapy is used at present, it is almost entirely confined to the application of cold sponges or to the use of packs. Personally, I believe that in

most cases the harm caused by the disturbance of the patient much more than offsets the good accomplished by such measures. Moving, turning, or otherwise disturbing the patient with pneumonia should be avoided so far as possible. Only the physical examinations that are required in order to follow the course of the disease should be made. Patients with pneumonia should never be allowed to sit up in bed in order to have their backs examined.

During recent years it has become more and more the practice to keep patients suffering from pneumonia, so far as possible, in the open air. This method undoubtedly has certain advantages, the chief of them being, in our opinion, that the comfort of certain of the patients is much increased. Occasionally in cases where the respirations are rapid, short, and labored, and patients are restless and distressed, moving them into the open air very quickly results in a marked amelioration of the respiratory distress and of the mental anxiety. Such patients certainly should be kept in the open air as long as they are comfortable and are relieved. Other patients, however, dislike very much to be put out-of-doors. They become more restless. They beg to be taken in. They dislike the necessary heavy clothing, and altogether they are much more uncomfortable out-of-doors than they are inside. With such patients we feel that it is a mistake to urge them to remain out-of-doors. If by enforced outdoor treatment the mortality of the disease could be reduced, there would be no question of the advisability of treating all patients, without exception, in this way. However, the method now has had an extensive trial. Certain very enthusiastic supporters have carried out the method to the fullest possible extent, but it yet remains to be demonstrated that the application of this method has resulted in any lowering of mortality. However, it has been abundantly demonstrated that the treatment of patients in the open air, even in the coldest weather, can be carried out with impunity.

The results, therefore, of our own observations and the reports of others have led to the adoption of the method mentioned above. For successfully carrying out the method certain provi-

sions are quite necessary. In the first place, it should be possible to move the patient from the warm room to the outer air without disturbing him or causing him to undergo any exertion. The clothing of patients should not be changed, nor should the patients be examined, in the open air. The bed coverings should be sufficient, the mattress should be thick, and the patients should be very frequently observed to see that they do not become exposed or cold. It is quite possible to allow them to sleep out-of-doors, provided they can be watched. Nurses looking after such patients should be cautioned to wear heavy clothing, for I have known more than one case of pneumonia to arise in nurses who have been unnecessarily exposed while caring for pneumonia patients out-of-doors. It is of very little value to produce a slight possible benefit to a patient at a great risk of making a healthy person ill.

The use of the various stimulating drugs has been so much debated that there remains no opinion to be expressed that is new, and practically no facts, new or old, to be presented. No one has made out a clear case for the employment of strychnin or camphor in this disease. Probably through every large hospital waves of strychnin enthusiasm and camphor enthusiasm have passed at intervals. I have heard teachers speak in the highest praise of each of these drugs and insist that they be given in all cases where stimulation was considered necessary. During the past three years, in the treatment of about 500 cases of pneumonia in this hospital, practically no strychnin, and very little camphor, has been employed. The results have shown that the mortality has not been increased by the omission of these drugs, and I feel sure, from my previous experience, that the course of the disease has not been unfavorably affected. It seems possible that in certain cases which I have observed previously, where very active and continued stimulation was employed, definite harm may have been done to the heart, but in regard to this I can only have an impression and have no definite data to offer.

I feel somewhat more uncertain about the advisability of employing alcohol in the treatment of pneumonia, but the im-

portance of its use in uncomplicated cases in persons not accustomed to the use of alcohol is very doubtful. In alcoholic subjects, especially those who have been constantly consuming large amounts, it is questionable whether all alcohol should at once be withdrawn. In such cases it is given for its mental effect and action on the nervous system rather than for any direct physiologic stimulating effect on the heart or respiration. Such effect alcohol does not have in any marked degree, and it is better, in my opinion, that alcohol should be given only to the cases with alcoholic history, and then in moderate amounts.

I have already spoken of the employment of digitalis in the early stages of pneumonia. It is on this drug, or drugs of this series, that we must rely in any hope of influencing the circulatory mechanism in pneumonia. In most cases of pneumonia digitalis is probably not needed. Both experimental evidence and clinical observations indicate that the toxic effects of pneumococcus infection are manifested rather in the respiratory mechanism of the body than in the circulatory organs. Nevertheless, in a number of cases the cardiac mechanism does show the effects of the intoxication, first by evidence of decreased cardiac strength and output of blood, and second, by disturbances in the regulatory mechanism of the heart. The studies of Cohn have shown that digitalis acts when fever is present just as it does when the patient has no fever, and also that its effects on the disturbed heart in pneumonia are exactly similar to the effects obtained on hearts similarly disturbed from any other cause. The statement that digitalis acts upon the heart which is suffering merely from insufficiency or disturbed power is difficult to prove, but the evidence becomes more and more convincing that digitalis does produce favorable effects in such hearts. On the other hand, when irregularities occur, or where signs of disturbances in the conducting system become manifest, such as in the case of flutter or fibrillation of the auricles, digitalis may be of very great value, even life saving. Cohn has shown that in a large number of cases of pneumonia fibrillation or flutter occurs at some time during the course of the disease. In these cases if digitalis effects can be promptly obtained, marked slowing of the heart

may be produced, and, associated with this, marked improvement in the patient's condition. In order to obtain such effects rapidly, however, either the patients must have been partially under the influence of digitalis before the drug is given, or the drug must be given in large doses intravenously. This latter method of administration, either of this drug or of strophanthin, which has been much used for this purpose, has been shown to be dangerous. This is especially the case when it is employed in a hospital where in many cases the history of administration of the drug before admission cannot be accurately obtained. On the other hand, by the method we have mentioned, giving moderate-sized doses of the drug early in the disease, we can very quickly obtain the desired effects when the actual need arises by the administration of the drug by mouth in comparatively small doses. If the need of the drug is quite evident, as much as 1 gram a day of digipuratum may be given by mouth. This method of administration gives the physician in charge at all times a feeling of confidence and security. His patient is in a position where digitalis action can be rapidly obtained without undue risks.

Among the most unfavorable symptoms which may arise during the course of pneumonia is the occurrence of abdominal distention. In certain cases it is merely the sign of gastro-intestinal disturbance, possibly decreased motility owing to involvement of the diaphragm. In most cases, however, where it is marked and severe it is one of the evidences of extreme and severe intoxication, and the paralysis of the bowels is probably central in origin. In the latter case the symptom is not of such serious importance in itself as it is as a sign of the gravity of the infection. It is true that abdominal distention, from whatever cause, has a purely mechanical effect which is unfavorable, namely, pressure upon the chest and thereby lowering of the area of lung space. For this reason, if no other, efforts should always be made to relieve this symptom. The proper application of stupes and the use of enemas in the milder cases usually bring relief. In certain cases temporary relief is obtained by the use of pituitrin given hypodermically, but I think its value has

been overestimated. In certain cases none of these measures will bring any relief. In these cases the distention frequently persists until *exitus* occurs. The time to treat abdominal distention is when it first occurs. It is a worrying and distressing symptom, and, if possible, should never be allowed to persist and reach a marked grade.

It is impossible here to speak of the treatment of the complications which may arise during the course of pneumonia. One of the chief duties of the physician should be to keep a sharp lookout for the onset of other focal infections, such as empyema, otitis media, etc. Much has been written concerning the danger of collapse at the time of crisis, and of the frequent occurrence of extreme prostration at this time, not infrequently ending in death. In my experience such a phenomenon is rare. I have seen few patients who caused alarm at the time a real crisis was taking place. I have seen certain patients die very shortly following what was thought to be a true crisis. It is probable, however, that the so-called crisis in these cases was merely an antemortem fall of temperature, such as occurs in other severe infectious diseases.

I have now discussed in a very brief way the non-specific treatment of cases of pneumonia. While in the cases due to pneumococci of Types II, III, and IV we are absolutely powerless, so far as affecting the micro-organisms themselves is concerned, and must rely merely on attempts to meet any physiologic accidents which may arise during the course of the infection, in the Type I cases we are possessed of a weapon which attacks directly the infecting organism and has no effect, certainly no beneficial effect, upon the physiologic processes of the patient. It is remarkable what a feeling of satisfaction it gives one to be possessed of a weapon with which one can attack directly such an insidious and powerful antagonist as the pneumococcus. As previously stated, the serum treatment of Type I cases should be undertaken at the earliest possible moment in the course of the disease, and the serum should be administered intravenously. The size of the dosage has been arrived at somewhat empirically. We believe that 90 to 100 c.c. of the serum, preferably diluted in salt solution, should be given, and that this should be repeated

every eight hours until a definite effect has been obtained. The exact mode of action of antipneumococcic serum in the patient with pneumonia is unknown, though studies of its action, both experimentally in animals and in the test-tube, have shown that it possesses certain properties upon which its power may depend. It has no bacteriolytic power or power to kill pneumococci directly. It has no demonstrable antitoxic power, though this may be because the toxin itself has not yet been isolated, but it has marked agglutinating power and it has the power of rendering virulent pneumococci susceptible to phagocytosis. It would lead us too far to attempt to discuss all the theories which have been advanced to account for its mode of action. It is sufficient to say here merely that it is antibacterial, meaning by this that the continued growth of the micro-organisms in the body is in some way prevented. Unless an extremely high grade of septicemia is present, usually one dose of the serum is sufficient to render the blood-stream free of organisms. In most cases the progress of the lesion in the lung is very quickly stopped. In our experience these two phenomena comprise the most serious features of the disease, the result usually depending upon the degree of invasion of the blood and the progressive character of the local lesion. In most cases, moreover, an early amelioration of the symptoms of the disease follows the administration of the immune serum. This has frequently been striking, and made evident not only by the patient's statement of his subjective sensations, but has been easily recognized by the improved mental condition, the slowing of the heart rate, and improvement in respiration. In certain cases following the administration of the serum there occurs an immediate sharp reaction which we have spoken of as a thermal reaction. In such a case, following within an hour of the administration of the serum, the temperature rises, sometimes several degrees. The patient may have a shaking chill. Following this the temperature rapidly falls, often to normal, profuse sweating occurs, and it is with this fall of temperature that the patient's condition shows marked signs of improvement. The signs are those of crisis. In certain instances the temperature remains low and improvement is

continued, and in a short time the patient is well. In other patients, however, the improvement only lasts a few to twenty-four hours, when the temperature again begins to rise. Such patients should receive treatment again immediately upon the appearance of increased temperature. For this reason patients showing this so-called thermal reaction should be very carefully watched, the temperature should be taken at least every two hours following the injection of the serum, and, as previously stated, treatment should be repeated whenever there is the least indication of return of the symptoms.

In other cases no such thermal reactions occur. The temperature, however, following the administration of serum becomes lower, the general condition improves, and usually in such cases following the second or third dose of serum the temperature reaches normal and the patient is well, the course in such a case having been that of recovery by lysis.

We have not believed that the thermal reaction in itself is of benefit to the patient, and have endeavored, if possible, to avoid such reactions by taking great care that the serum is given slowly, at body temperature, and that the serum is perfectly clear and contains no sediment. It has not been possible, however, to avoid such reactions completely, even though the greatest precautions are taken. Reactions, however, in our experience have not been of any serious import. They are probably independent of the antibody content of the serum, but, as is known, may occur upon the injection of any foreign protein substances into the circulation.

Certain observers who have treated pneumonia patients with immune serum have laid much stress upon the occurrence of so-called serum reactions or serum disease. Serum disease in its typical form consists of a group of symptoms, namely, fever, skin rashes, glandular enlargement, joint pains, and edema of the skin, occurring seven to fourteen days following the administration of the serum. Such typical serum disease, however, is not the rule. Usually these symptoms may appear isolated or in groups, occurring any time from within a few hours to a month following the administration of the serum. They may disappear, only to again recur, and the whole course of the symptom-

complex may be quite irregular and bizarre. Certain of the features, especially urticaria and itching, may be distressing to the patient. The occurrence of fever and other symptoms may cause the physician anxiety as to the etiology, but, except for this, serum disease is of little significance. It practically never has a fatal outcome, and so far as we know all the disturbances are recovered from; even the evidence of disturbed kidney function, which occurs in about 10 per cent. of the cases, disappears and no trace of the disturbance remains. It seems a mistake, therefore, to lay undue stress on the possible occurrence of this complication, provided the administration of the serum is of value. That it is of value in cases of pneumonia due to Type I infection is made evident by the facts that we have previously mentioned, namely, that the septicemia is caused to disappear, the progression of the lesion of the lung is stopped, but, above all, by the fact that in our experience the mortality in this type of infection by the use of this method of treatment has been markedly reduced. Whereas before treatment of this type of pneumonia by serum was undertaken 25 per cent. or more of our cases died, in the last 108 cases treated with serum in the Hospital of the Rockefeller Institute there have been but 8 deaths. If the statistics continue as satisfactory in cases of pneumonia treated in the future, it is evident that by this method 8 or 9 out of every 100 cases of pneumonia that would otherwise die can be saved. This is a result worth working for and worth going to a good deal of trouble to bring about.

The application of this method requires considerable effort and attention to details, and is complicated, judged by the standards of drug therapy. At the present time, however, it represents the only satisfactory method of specific therapy in this disease. An ideal therapy would undoubtedly consist in the use of a drug administered by mouth, having specific bactericidal action upon pneumococci in the body. The discovery of a quinin derivative, ethylhydrocuprein, offered promise of being such a drug, since it has a specific bactericidal action upon pneumococci in the test-tube and can be given to patients in sufficient doses to endow the blood with specific bactericidal properties. However, the size of the dosage required to bring about this reaction is very close to the

toxic dose, and even with the greatest care in the administration of the drug certain patients suffer from the toxic effects of the drug, especially upon the eyes. Moreover, the action of the drug upon pneumococci is not instantaneous, and, with the concentration of the drug which can be obtained with safety in the blood of the living patient, the time required for bactericidal action is considerable, so that in certain instances, although the blood removed from the body and placed in the test-tube has a direct bactericidal action upon pneumococci, nevertheless pneumococci may be growing in the same blood within the body. For these and other probable reasons the actual clinical results from the use of this drug have been very disappointing. Over 75 cases have now been treated and most carefully studied, and the evidence which we have obtained does not justify recommending the use of this drug in a routine manner in the treatment of lobar pneumonia. An indication, however, has been given of a possible future ideal method of treatment, and sufficiently good experimental results have been obtained to indicate that an analogous form of treatment is not an impossibility.

To state briefly our position at present in the treatment of acute lobar pneumonia, we believe that, first, all cases suffering from pneumonia due to pneumococci of Type I should be actively and thoroughly treated with the homologous immune horse-serum; second, all cases of pneumonia should receive careful nursing and intelligent watchfulness on the part of the physician. The toxic effects of the infection upon the heart and circulatory system can be best met by the judicious and prompt use of digitalis. The use of other drugs, so-called cardiac and respiratory stimulants, is of doubtful value. The use of morphin in patients with restlessness and the use of alcohol in alcoholic subjects is of value. Hydrotherapy and so-called aërotherapy should be used with moderation and with discretion. The object of both is to conserve the patient's energies and to make him more comfortable, but upon the infection itself probably neither method has much effect. Finally, we possess at present no drug which has a specific action upon this severe and important infectious disease.

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THE CLINICAL PHARMACOLOGY OF DIGITALIS

The Action of Digitalis Discussed in the Light of Experimental Data and of Clinical Observation as it Affects the Rate of the Ventricles, the Blood-vessels, and the Kidneys. Attention is also Called to its Effect on Dyspnea, Cardiac Pain, and Indigestion in Heart Disease. A Note is Added on the Action of Digitalis in Pneumonia.

During the past few years, as Hewlett has recently pointed out, there has developed an increasing appreciation of the fact that the data ascertained in laboratories devoted to academic pharmacology are not immediately available for use in clinical procedure. The indications for the use of digitalis in clinical medicine have been seriously confused on account of failure in the attempt made by many clinicians to harmonize pharmacologic results with experience in patients. The difficulty is natural when one considers the factors which have provided the ground for confusion. In the first place there is the question of species, and second, the question of dosage. As among species, there is a wide difference in tolerance, so that the lethal dose for one may be many times that in another, and even in the same species the variation in the lethal doses from one animal to another is subject to large fluctuation. But in preparing experimental data for clinical use there are other difficulties as well. A very important one concerns the criterion to be looked for; is it brought about by a small dose corresponding to therapeutic limits, a larger one to bring out toxic effects, or is it so large as to result in death?

So far as digitalis is concerned, experiments have shown apparently a wide variety of results, with doses possibly in therapeutic limits, depending on the tissue, heart muscle, or smooth arterial muscle studied. And among the arteries themselves differences with the same dose are reported to exist in the behavior of renal and intestinal vessels. Finally, for the purposes of standardization of the drug itself, it is always the lethal dose which is taken as the criterion of comparison. There can be no just criticism of this practice, so that it is understood that although different lots of the drug may be so compared, the dose obtained has no necessary relation to therapeutics.

These considerations suffice to show the importance of another method for studying drugs, and especially for studying digitalis. In experiments many of its effects have been described, but the purposes in clinical medicine for which it is prescribed are limited to a few of these effects. Practically these can now be studied in the human patient with as much facility and as great a degree of accuracy as until now in the experimental animal. The study can be carried on not only without prejudice to the patient, but to his distinct advantage. Most important of these are its effects on the heart; second, its effect on the blood-vessels; third, its effect on the kidneys. Clearly, in heart disease or in circulatory distress, there are symptoms of which complaint is made based on the derangement of other functions besides those due to the organs mentioned, such as refer to breathing, to thoracic pain, and to digestion. Important as they are, their functional relations are difficult to define and offer unreliable criteria for judging of the drug's action. We shall, however, return to their consideration.

With increasing knowledge of the functions of the heart, the varieties of derangements which are recognized have increased in number, so that it is no longer possible to speak of heart disease as a unit, even if the varieties of valvular disease are excluded. The heart in ill health, for instance, may vary as to its mechanism (see table on p. 565), in itself a fundamental consideration. Next the heart is obliged to act in the presence of a variety of conditions of the peripheral circulation. Finally,

the kidneys' function play an important rôle in defining the condition of a patient.

A. Rhythm. (Rate)	B. Pressure.	C. Edema.
Sinus rhythm	Low:	Without edema, 1
		With edema, 2
	High:	Without edema, 3
		With edema, 4
Auricular fibrillation	Low:	Without edema, 5
		With edema, 6
	High:	Without edema, 7
		With edema, 8

If these three factors—rhythm, pressure, and edema—are considered, at least eight groups of cases result, for each of which it may be necessary to study separately the effect of giving digitalis.

So far as concerns the action on the heart, it is often desirable to obtain other effects besides one on the rate of the ventricles. For even if the ventricular rate is slow, as it is in heart-block, even when it is not inordinately slow, the circulation may be obviously failing. We may then give digitalis in the hope not of slowing the rate further, but of improving the contractile power of the muscle so that by a greater degree of shortening more blood can be expelled into, and more effectively propelled through, the periphery. In experiments it has been possible to show that heart muscle under the influence of digitalis shortens; we are, therefore, on sure ground so far as that fact is concerned. Whether it does so in the doses we give to patients is not quite known. It is inferred to occur because the impression exists that improvement in general well being is admitted by patients, but for establishing the point there is no objective method. But that there is a muscular effect we know, even though we do not know that the effect is one of increased shortening. The evidence for the muscular effect referred to is found in the elctrocardiogram, and consists in an alteration in the ventricular representative or complex. An upward T-wave becomes inverted; an inverted T-wave changes to an upward one. It is now generally agreed that this change has a muscular rather than another cause, for we associate the electrocardiogram mainly and especially under

these circumstances with muscular action. An improvement in circulation apart from an effect on rate is looked for now, we think justly, both because of carefully ascertained subjective symptoms and also because of the electric change just described. So far as is known now, there is no reason to doubt that digitalis always affects heart muscle. When the effect fails to be apparent, one of two reasons may possibly be assigned. First, in health or where a maximum circulation already exists; under such circumstances an alteration in the patient's well being is not to be detected. But even in him the electric change is found. Second, at the other extreme of the scale, where heart muscle has become so far lengthened or stretched that shortening or improved contraction to an extent to be useful no longer can take place, even here the electric phenomenon takes place. This, then, is the evidence for muscular action.

One of the commonly accepted results of digitalis action concerns the reduction of ventricular rate. A distinction must be made here between ventricular rate when the auricles are behaving normally and when they are fibrillating. So far as concerns the effect when the auricles are fibrillating there is no discussion; their impulses can be blocked, with a consequent fall in ventricular rate. This result can regularly be obtained and the rate reduced to almost any desired level, depending on the size of the dose. On occasion, symptoms referable to the stomach unfortunately arise, but these are usually not sufficiently important to interfere with the success of treatment. But the effect of digitalis on the rate of the ventricles when they beat in sequence with normally contracting auricles is another matter. A rule under these circumstances is difficult to formulate. But one may say that in adults when the rate of the auricles is within normal limits and there is no edema that no reduction in rate takes place unless auricular impulses are blocked; in this event there is no true reduction in rate. But when the auricular rate fluctuates sharply, or when edema is present, or when the rate is elevated in association with the presence of edema, giving digitalis often is followed by slowing. The matter may be put briefly by saying that in health, when the circulation is normal,

no reduction of rate follows the giving of digitalis; in disease, in the conditions mentioned, it may be expected.

The effect of digitalis on the peripheral circulation, measured in terms of blood-pressure, is a subject in debate. In experiment, large doses are known to elevate pressure. But in normal persons and in heart disease when the level of pressure is within normal limits, a change of pressure level probably does not take place. There are types of cases, however, in which pressure falls, and there are notably two of these. The first concerns cases in which there is no edema, but an elevation of pressure to a level as high as 200 mm. Hg. With improvement in the general circulation, whether this occurs as the results of enforcing rest in bed or of giving digitalis, the level of pressure often falls, even as much as 30 mm. or more. Frequently the pressure in cases of this type, even though it falls for a time, returns to its former level, whether or not the treatment continues. The second type concerns cases with high pressure and edema. Giving digitalis is accompanied almost regularly by a fall in pressure when the edema disappears. The level usually stays low if the patient is not suffering from chronic vascular hypertension. If he is so afflicted, the pressure after having fallen tends again to rise and to reach its initial level, whether or not the treatment continues. In these statements relating to the subsequent behavior of pressure after digitalis therapy it is understood that other methods of treatment may bring about a fall of pressure.

When blood-pressure is high, current teaching has warned against the administration of digitalis. If there is associated with high blood-pressure a degree of heart failure manifested either as edema or as a more vague group of symptoms, one does not hesitate to prescribe digitalis. Indeed, as has just been shown, a fall rather than a rise of pressure must be anticipated. How often digitalis actually raises the level of pressure already high and brings about cerebral apoplexy in consequence is scarcely known with accuracy. One may doubt the frequency of such an occurrence, and in the absence of sufficiently precise knowledge not be deterred on this account from its administration. The experimental basis on which this fear is founded is not yet sufficiently con-

vincing, nor does clinical experience, where exact knowledge is available, indicate that this accident is probable.

The effect of digitalis on the kidneys, that is to say, its effect as a diuretic, is reputed to be important. A decision as to whether digitalis actually has this effect is difficult. The flow of urine has in experiment in normal animals been shown to increase. But an increase in the outflow of urine probably does not occur in the normal human being or in one in whom there is no edema. It need scarcely be said, in judging of the presence of edema, that a slight degree of edema readily escapes examinations even more than cursorily detailed. On the contrary, should digitalis administration be urged to the point of gastric discomfort where the intake of water is diminished, a diminished urinary outflow dependent on the diminished intake results. The effect of giving digitalis when edema is present is quite different. Especially in cases which are not long standing the administration of the drug is followed promptly by the excretion of large quantities of urine. And usually on each occasion when the edema reaccumulates the result of giving digitalis is equally fortunate. Occasionally other drugs, such as diuretin and theocin, are more effective. An accurate account of the clinical pharmacology of these must be found elsewhere. Occasionally also in cases in which it has usually been effective digitalis fails for a time to act. We are in the habit, whether justifiably is still not sufficiently determined, of ascribing failure at such times to alleged renal fatigue. At all events, although digitalis fails on one occasion, on another, removed a period of time, it may and usually does succeed. Whether the increased output of urine depends on a specific renal action of digitalis, and if so, whether its action is on renal epithelium or vascular tissue, may so far as exact clinical observation is concerned be a subject still open to investigation. A decision involves a precise estimate of how far the action of digitalis on heart muscle, and the consequent improvement in the rate of flow of the circulating blood, is responsible for the general result. That the effect may depend on the action of digitalis on heart muscle alone is shown in a study of those cases in whch general edema, associated with orthopnea, disappears without

any alteration in the rate of the heart; the rate being maintained at a constant low level (60 to 70) throughout both the edematous and the edema-free states.

It is clear that in any category (5 to 8 in table on p. 565) in which the auricles fibrillate, whether the pressure be high or edema present, digitalis or a member of its group must be given. No other drug is a substitute for it.

The symptoms referable to breathing, to position, to thoracic and referred pain, and to digestion are more difficult to deal with. They are practically withdrawn from exact objective description or measurement. Where these symptoms depend upon a failure of heart muscle and where heart muscle is still in condition to be affected by digitalis, a general improvement in the circulation depending on the muscular action of digitalis is accompanied by the disappearance of these disabilities. A striking instance relates to the diminution in the disability due to the position in lying, when this is the only substantial symptom of which complaint is made. A most difficult symptom to appraise relates to pain. Where this is due to exertion, especially exertion immediately associated with the onset of pain, success in its relief is usually associated with the treatment of the heart muscle. That pain which is independent of exertion and to which alone the term "angina pectoris" should be applied is not discussed in this connection.

A problem of interest is attached to the question of the action of digitalis in acute infectious diseases, and especially in those stages where stimulation of the circulation is apparently desirable. It is important to point out that the time has passed when infectious diseases may be grouped together and considered as one. In immunity, striking and fundamental differences have already been shown to exist among them. In the pathology of heart muscle differences no less striking may be shown to exist, especially during the initial and early stages of the diseases. It is sufficient to name the focal necroses of typhoid fever, the early gumma or gummatous infiltration in syphilis, the miliary nodules in rheumatism, to mention only a few of the better known specific lesions. Nor may we speak of the action of digitalis as common to them

all. Until now an exact study of the action of digitalis has been made only in pneumonia. In this disease no constant specific pathology is known. But pneumonia, that is to say, lobar pneumonia has been especially singled out for controversy so far as the action of digitalis is concerned. Many, and among them the best clinicians, have failed to observe the efficacy of digitalis action; others no less eminent have asserted its beneficial action. The controversy made no progress in the absence of exact criteria.

At the Hospital of the Rockefeller Institute we have accordingly studied the action of digitalis in pneumonia primarily with the view of determining whether it was active here as in the absence of fever; second, whether, if it were active, its effect is beneficial. Electrocardiograms were made frequently, daily or oftener when possible. The criteria employed were three; first, the change in the form of the T-wave already noticed; second, the lengthening of the auriculoventricular interval, a well-known and constant result of digitalis administration; third, a reduction in ventricular rate when the auricles fibrillate or flutter. It may be said at once that, as in the non-febrile, digitalis does not alter the sinus rate of the heart. We found, briefly, that digitalis acted in pneumonia, for it altered the sign of the T-wave and lengthened the duration of the auriculoventricular interval, occurrences which did not take place in patients not receiving digitalis, and it reduced the rate of the ventricles while the auricles were in a state either of fibrillation or of flutter. These effects were all noticed during the presence of fever. Based on the criteria used, then, the conclusion is justified that digitalis acts in the febrile period of pneumonia. A beneficial action, we think, is shown in the action of digitalis in the cases in which the auricles flutter or fibrillate. This irregularity occurred in 12 of 123 (9.7 per cent.) accurately studied cases. When it occurs the symptoms of collapse usually supervene; the condition of the patient is grave and the outcome of the disease doubtful. The ventricular rate frequently rises abruptly from the usual level of 90–110 to 160–190. The higher rate is by no means uncommon. Should the irregularity and the high rate persist and re-

main untreated, a fatal outcome must usually be expected. These cases can be and often are saved by the timely reduction of ventricular rate brought about by giving digitalis. The reduction in rate may be remarkable. In one patient in whom the ventricular rate was 184, it was reduced to 84 by the action of this drug. This rate was actually lower than that which prevailed when the normal sinus rate was restored (130). Rate, consequently, can actually and beneficially be controlled when fibrillation of the auricles is present. Fibrillation need not, therefore, be an occurrence associated with danger to the patient. One may, indeed, in view of the facts related, regard its onset as in a sense useful in controlling the patient's circulation. If digitalis did not act in pneumonia, most of the patients subject to this disorder would probably succumb.

On account of the frequency with which fibrillation or flutter of the auricles occurs, we have introduced in the hospital of the Institute the routine administration of digitalis in pneumonia:

Days of disease.	0	1	2	3	4	5	6	7	8	9
If seen early....		0.5 gm.	0.5			0.5	0.5			
If seen late....					1.0		0.5	0.5		

If seen early, we give by mouth 0.5 gram on the first and again on the second day. We give it again on the fifth and sixth days. We give no more unless an indication arises. The patient is considered digitalized; if fibrillation or flutter develops, we do not expect this rate to rise, but instead either to remain constant or to fall. If the patient is seen later, on the third or fourth day, we give 1 gram in the first twenty-four hours, then wait a day, and on the two subsequent ones give 0.5 gram on each. Then, as in the first case, we give no more unless an indication arises. Should fibrillation or flutter set in, and should the rate unexpectedly rise, we continue to give digitalis until the desired fall in rate occurs, for the danger from digitalis intoxication is less than from the circulatory disturbance. Large doses (up to 3 and 5 grams) may be necessary, for exact study has shown that susceptibility varies among individuals in a range on occasion as 1 : 5.

No recommendations are made here on the question of the administration of digitalis preparations intramuscularly or intravenously. Exact knowledge on its action is wanting. The warning is, however, gravely expressed that digitalis should under no circumstances be given to a patient who has previously been given digitalis in any form or by any route. The failure to obey the warning has on many occasions been followed by disastrous results to the patient.

CLINIC OF DR. E. LIBMAN

MOUNT SINAI HOSPITAL

SOME GENERAL CONSIDERATIONS CONCERNING AFFECTIONS OF THE VALVES OF THE HEART[1]

BEFORE discussing the subject of the symptomatology of cases of subacute streptococcus endocarditis (so-called "chronic malignant endocarditis") it will be necessary to impress upon you the important distinction that must be made between cases of valvular defect alone and cases of endocarditis occurring with or without a previous valvular disease. The lack of sharp differentiation of these two conditions and the use, particularly the loose use, of the term "chronic endocarditis" has led to much confusion and to many inaccuracies in diagnosis.

A valvular defect is a quiescent lesion the result of a previous diseased process of the valve. The causes of such valvular defect are as follows:

I. Rheumatic endocarditis.
II. Syphilitic endocarditis.
III. Atherosclerosis.
IV. Congenital defects.
V. Traumatic lesions.
VI. A previous bacterial infection, with recovery.

There is so much confusion at the present time concerning what our conception of rheumatic fever or rheumatism should be that I believe it important to give you what I conceive to be the proper delimitation of that term today. Rheumatism is characterized by pain, swelling, and redness of the joints, accompanied by fever. There is a tendency for the infection to

[1] Remarks made as an introduction to a series of demonstrations of cases of subacute streptococcus endocarditis in the wards of Mount Sinai Hospital, New York City.

jump from one joint to another, and suppuration does not occur (except perhaps rarely, due to a secondary infection). The disease is apt to occur in association with or to be preceded or followed by chorea, tonsillitis, endocarditis, pericarditis, and cutaneous lesions.

The endocarditis is of a special type, as I shall later explain to you. It and the pericarditis are usually associated with the presence of peculiar foci in the heart muscle which are submiliary in size and which are called "rheumatic nodules." These are to be carefully distinguished from the subcutaneous nodes that occur in rheumatism, notwithstanding the opinion of Chiari that the lesions are the same in both. These lesions were first described by Aschoff, and are usually called "Aschoff bodies," or, more correctly, according to Aschoff himself, "the Aschoff-Geipel bodies." It has been claimed that these bodies have been seen in the voluntary muscles (Huzella) and the fronto-occipital fascia (Tilp). These focalized lesions are found in the endocardium, in the interstitial tissue of the myocardium, but most often near the small and medium-sized blood-vessels, to the adventitia of which they have close relationship. According to Aschoff, they are derived from connective tissue. In subacute streptococcus endocarditis there are also focalized lesions found in the heart, but these are different in location and entirely different in structure from the Aschoff bodies (the so-called Bracht-Wachter lesions).

The Aschoff bodies are not present in all cases of verrucous endocarditis following typical rheumatic fever. The absence is, however, exceptional, being noted only twice in the cases that we have studied. Only recent Aschoff bodies should be considered in attempting to establish the diagnosis of a recent rheumatic infection. True Aschoff bodies have hitherto not been produced experimentally, nor has the typical verrucous endocarditis of rheumatic fever. The Bracht-Wachter lesions have been duplicated by a number of investigators by injecting cocci cultured from the blood or the vegetations of cases of subacute streptococcus endocarditis. Bacteria cannot be demonstrated in Aschoff bodies.

Notwithstanding the large amount of work that has been done in recent years in an attempt to find the etiologic agent in rheumatic fever, I am not convinced that the cause of the disease has been found. As you know, streptococci have been found by a number of investigators in the blood and less commonly in the joints and endocardial lesions. These streptococci vary considerably; most are anhemolytic. You will find an accurate description of them and the details of the differences between them in an admirable paper on streptococci and pneumococci, just published by Dr. Aschner in the Journal of Infectious Diseases.

We were enabled to study some of the cocci cultured by a number of investigators from cases of arthritis classed by them as rheumatic fever. They all showed suggestive variations from the anhemolytic streptococci isolated by us from cases of subacute streptococcus endocarditis. For convenience of comparative description I have been in the habit of grouping the anhemolytic streptococci isolated from cases of subacute streptococcus endocarditis as "endocarditis cocci," and those isolated by various observers from arthritis cases as "arthritic cocci."

These are differences in morphology and in the presence of capsules and their persistence. Of greater interest, and this also holds true of a hemolytic streptococcus that was sent to us by Dr. Rosenow, and which was isolated by him from a case of supposed rheumatism, is the difference in the amount of precipitation produced by these cocci when grown on media containing glucose and serum. Many years ago I pointed out that all streptococci throw down a heavy precipitate in fluid media containing glucose and serum, and in solid media cause a remarkable diffuse whitening of the medium. This action is due to acid production. The degree of whitening produced by the arthritic cocci is so much more marked than that produced by the endocarditis cocci that one can with ease differentiate the tubes in which they are inoculated from those that were inoculated with the endocarditis cocci.

The cases in which streptococci have been found in the blood in cases of supposed rheumatic fever can for purposes of critical study be divided into three groups:

1. Cases with a definite primary focus other than the tonsils (and with this are grouped the adenoid tissue in the nasopharynx or base of the tongue). Such cases should not be classed as rheumatic fever. The clinical conception of rheumatic fever is that of a disease having no primary focus other than that in the adenoid tissue of the throat. It is even possible that the throat lesions in rheumatic fever may not represent the portal of entry, but may be the first (or at times the only) clinical manifestation of the rheumatic virus.

Cases in this first group should not be called rheumatism, but should be described as streptococcus arthritis, or anhemolytic streptococcus arthritis. Such cases are no more to be classed as rheumatism than are cases of arthritis secondary to an otitic or other focus set up by hemolytic streptococci. The latter cases have always been called "streptococcus arthritis." It is not superfluous to emphasize this point—the numerous errors in the literature of the last years make it essential.

2. Cases without a primary focus other than tonsillar, without evidence of endocarditis or pericarditis. Some of these cases, I believe, are instances of general streptococcus arthritis of tonsillar origin, and some are instances of true rheumatic fever. The first type should again be called "anhemolytic streptococcus arthritis," and the second type, "rheumatic fever." The significance of the streptococci found in the second type is the same as in Group 3.

3. Cases which must be considered as true rheumatic fever. The most important study in this group is that made by Swift and Kinsella. They found streptococci in the blood of 8 out of 52 cases of rheumatic fever. Even if one were unwilling to group all the cases with positive findings as rheumatic fever, the percentage of positive results is very small. Furthermore, the bacteriemia when present was fleeting. The main fact is that in their material were instances of arthritic disease in which endocarditis or endocarditis and pericarditis developed, and in which, at autopsy, lesions characteristic of rheumatic fever were found.

The authors themselves regard the streptococci as secondary

invaders. The complement fixation tests all proved negative even when the serum was tested against the homologous organism. In cases of subacute streptococcus endocarditis the complement fixation test is practically always strongly positive when tested against the homologous organism. Furthermore, in the latter disease the cultures of the blood are nearly always positive. If a streptococcus were the cause of rheumatic fever, why should an organism so easily grown in the cases in which it is found not be more frequently capable of isolation?

If the evidence at our disposal at the present time is insufficient to convince us that the streptococci found in cases that we are willing to accept as instances of rheumatic fever are the cause of the disease, how are we to regard the organisms found in such cases? They may represent unimportant secondary invaders, or they may at least at times be significant of a mixed infection. What I mean to convey is that in some cases we may be dealing with rheumatic fever with or without rheumatic endocartitis, and with subacute streptococcus endocarditis. I am led to believe that such a condition may exist because I have seen at least one instance of such mixed infection of the valves of the heart. I shall describe this observation later today.

For purposes of study of the etiology of rheumatic fever it is important that future students depend mainly upon the results of investigations before and after death of cases of rheumatic fever in which verrucous endocarditis, or pericarditis, develops, and in which recent Aschoff bodies are found in the heart muscles. The investigator can then be sure that he is studying cases that cannot be interpreted otherwise than being cases of rheumatic fever. It is important to exclude cases with lesions on the valves due to such a mixed infection as I have mentioned to you. I have studied a number of such cases with entirely negative results as regards the presence of streptococci.

Rheumatic infection is the most common cause of valvular defects, the end-results being the stenoses and insufficiencies with which you are familiar. I shall later demonstrate to you some of the intermediate stages between the recent endocarditis and the final stenoses or insufficiency. You will be surprised

to see how frequently the tricuspid valve shows an organic insufficiency or a stenosis of rheumatic origin. The lesion of the tricuspid valve often involves only part of its circumference, and that is why many cases of organic disease of the valve are overlooked.

Syphilis, as you know, involves the aortic valve with greatest frequency. How often it involves the mitral valve we do not definitely know. The mural endocardium is occasionally affected. Syphilis is a close second to rheumatic fever in the production of valvular defects.

Atherosclerosis, an essentially degenerative lesion, causes insufficiencies and obstructions of the aortic valve. The mitral valve is much less frequently involved, the process often beginning in or near the auriculoventricular ring rather than at the free margin of the flaps. Obstructions and insufficiencies may be produced.

The defects produced by congenital disease I shall not discuss today. I have seen one case of valvular defect due to trauma. That was a case of healed rupture of an aortic flap in a man thirty-three years of age. The injury occurred in childhood. The occurrence of a valvular defect resulting after recovery from a bacterial infection of a previously healthy valve I shall discuss later.

The varieties of endocarditis are:

1. Rheumatic.
2. Syphilitic.
3. Bacterial.
4. Terminal (verrucous).
5. Indeterminate.

The endocarditis produced by the virus of rheumatism is a typical one—always verrucous when fresh. The lesions are small and firm and, under the microscope, are found to be covered by endothelium. On section, bacteria have rarely been demonstrable, and then in very small numbers; the only organisms found in the sections or in culture (the latter more infrequently) were streptococci. I have never found bacteria in the lesions.

The infection occurs in acute, subacute, and recurrent form.

If recurrences are close together, one could speak of a chronic rheumatic endocarditis. In the first attack the virus generally infects a healthy valve, in this way differing sharply from the infecting agent in subacute streptococcus endocarditis, which, in nearly every instance, involves a valve already the seat of a valvular defect.

The rheumatic virus attacks most often the mitral and aortic valves, and less commonly the tricuspid valve. I have just told you that organic disease of the tricuspid valve is far from uncommon. Practically all such cases are rheumatic in origin.

As regards syphilis, we know clinically practically only the end-results. It is very probable that it will be found that the disease can occur in acute, subacute, or chronically recurrent forms. As far as we know, it usually attacks a previously healthy valve.

We now come to the cases of endocarditis that I group together as bacterial. You may ask me why I do not include the rheumatic cases in the bacterial group. The answer is that it has not been proved that the virus is bacterial. If it should be demonstrated that it is, the rheumatic cases would be included in the bacterial group, and be characterized by the name of the infecting organism. Until the cause of the disease is found, it is best that we characterize it by the clinical appellation.

Among the bacterial endocarditides we have, first, the cases of acute endocarditis (the previously so-called "acute malignant endocarditis") which is nearly always engrafted upon a previously existing valvular defect. This type of the disease is most commonly due to hemolytic streptococci, pneumococci, staphylococci, the influenza bacillus, and the gonococcus. A number of other organisms have been less commonly found in this disease; these are mainly the meningococcus, the Micrococcus endocarditidis rugatus, the Micrococcus flavus, spirilla, actinomyces, etc. Rarely an anhemolytic streptococcus infection may run an acute course. Since it has again been found in recent years that Gram-negative organisms like the Micrococcus endocarditidis rugatus of Weichselbaum and the Micrococcus flavus can be found in cases of endocarditis, it is very important that all Gram-

negative cocci found in the blood-current be studied very carefully. If there be present an acute urethritis or a cerebrospinal meningitis, it may be easy enough to come to a conclusion as to the character of the infecting organism, but if a Gram-negative coccus is found in the blood and one of these two conditions is not present, it will not do to simply call the organism the gonococcus, as has often been done in the past, and say that the case is one of general gonococcus infection without determinable primary focus.

Nearly all cases of acute bacterial endocarditis end fatally. More recoveries have been described when the gonococcus was the invading agent than when any of the other organisms was found. When a patient recovers from such an infection he may be left with a valvular defect. Dr. E. G. Janeway published a remarkable case of gonococcus infection of the pulmonary valve with recovery, the man developing a pulmonary insufficiency.

It is important to realize that we do not at the present time know how often or whether a patient can have an acute bacterial infection of the valvular apparatus of the heart and go on to recovery without leaving any evidence of cardiac damage. Postmortem experience indicates that if such a condition of affairs does occur, the frequency must be minimal compared to that which we know exists in cases of subacute streptococcus endocarditis.

The second group of cases due to the bacteria, that can with more or less ease be cultivated by our present methods, runs a long course. Its duration is measured by months, while that of the acute type is measured by weeks. The usual duration is four months to two years or more. The only cases that could at all be termed "chronic" are the longest ones. Most of the cases are more properly called "subacute."

Those of you who have read much on this disease will have noted the great variety of names by which it has been designated. It is the old "chronic malignant endocarditis." Some of the other names are: chronic septic endocarditis, septic rheumatic endocarditis, chronic infectious endocarditis, chronic ulcerative endocarditis, endocarditis lenta, etc.

Cases of subacute bacterial endocarditis are much more common than cases of the acute form, but not nearly as frequent as rheumatic and syphilitic affections of the valves. I have seen in the hospital and in consultation practice over 250 cases. The condition is due to anhemolytic streptococci in over 95 per cent. of the cases. The majority of the remaining cases is due to the influenza bacillus. Other organisms, particularly the gonococcus, can rarely cause a subacute clinical picture.

It is interesting to note that in these subacute cases there is not infrequently toward the end of the disease a secondary infection by pneumococci. When this occurs it is usually due to an intercurrent lobar pneumonia.

We have observed one case that is, from the standpoint of etiology and clinically, of great importance, namely, a mixed infection by the virus of rheumatism and an anhemolytic streptococcus. In the heart from this patient, in whose blood during life there had been isolated abundant colonies of anhemolytic streptococci, there was found a large vegetative lesion of one of the aortic flaps which on section was found to be practically one mass of streptococci. On the mitral valve was found the fine beaded lesion characteristic of rheumatic infection. In these vegetations there were no bacteria found either in crushings or on section. The heart muscle contained abundant Aschoff bodies.

Combinations of subacute streptococcus infections of the heart valve and other condition are not rare. The combination with general miliary tuberculosis is a particularly striking one. I have seen at least two such cases at postmortem examination. It is to be noted that anhemolytic streptococci may occur in the blood in cases in which neither an endocarditis nor an arthritis develop. The finding of an anhemolytic streptococcus in the blood of a patient does not spell "endocarditis." This holds true even if there is a valvular defect present. However, it must be admitted that under the latter condition one could not clinically absolutely exclude an endocarditis. I have seen a number of cases of valvular disease in which bacteremia of one kind or another arise from a primary purulent focus, and in which no recent lesion was found on the valves of the heart or on the

mural endocardium. Such cases I have usually designated "valvular defect with intercurrent bacteremia."

It is a peculiar fact that the primary focus in cases of acute bacterial endocarditis is usually a very active and often an extensive one, and may be found in any part of the body. In cases of subacute streptococcus endocarditis it is almost the rule that no very active primary focus is evident. Generally such cases are to be ascribed to older or, most commonly, latent infections of the accessory sinuses, or some structure in the mouth or nasopharnyx (teeth, gums, tonsils). Some authors believe that the invasion may occur at times from the intestinal tract where anhemolytic streptococci are normally present.

In both the acute and subacute varieties the aortic and mitral valves are the most frequently involved. The pulmonary and tricuspid valves are much less commonly affected. In the subacute cases the involvement of the right side of the heart is very rare. The lesions in both the acute and subacute cases vary from small to very large vegetations, which are usually friable. In them are found enormous masses of bacteria, in striking contrast to the bacteria-free lesions in rheumatic endocarditis. Ulceration of valves may occur in both forms, but is much less common in the subacute. In the latter cases such ulceration occurs almost solely in the aortic valve. Infection of the mural endocardium is much more common in the subacute cases, and when the mitral valve is involved there is often a characteristic, almost pathognomonic, pathologic picture produced by the peculiar involvement of the wall of the left auricle and the chordæ tendineæ which are not infrequently ruptured. Embolic aneurysms are more common in subacute cases.

I have told you of some of the differences from a bacteriologic and pathologic standpoint between rheumatic and subacute streptococcus endocarditis. A few of the clinical distinctions will interest you. I have never seen iritis or iridocyclitis in the non-rheumatic type of disease. Acute pericarditis is very rare in subacute streptococcus endocarditis and frequent in rheumatic endocarditis. Erythematous cutaneous lesions (erythema multiforme) may occur in cases of subacute streptococcus endocarditis,

but erythema nodosum I have not noted. Arthritic swellings may occur, but it is rare to see a real, actively swollen, red joint. When acutely inflamed joints or an acute pericarditis occurs, one must keep in mind the possibility of a mixed infection with rheumatism. That such a mixed infection can occur you now know.

A very small number of undoubted cases of subacute streptococcus endocarditis in which the streptococci have been isolated from the blood have become bacteria free under observation and have been described as having recovered, Unfortunately, in the cases recorded in the literature, no later reports have been given stating whether the patient had been again examined to determine whether or not the phenomena which I have described as occurring in cases that have become spontaneously bacteria free were found. I have seen 3 cases in which the streptococci disappeared and complete recovery ensued. One of these cases has been watched over a prolonged period. This case was studied by Dr. Louria, of the Brooklyn Jewish Hospital, together with his assistants, Dr. Blatteis and Dr. Rosenthal, one of our former interns. In this case there were five positive cultures, as many as 200 colonies of an anhemolytic streptococcus to the cubic centimeter of blood being found in one of the cultures. There were ten later negative cultures. The patient has been well for over three years and there are no residua. I have been hoping that Dr. Louria or one of his assistants would publish this case in extenso. It was a great privilege to see this case a number of times, and I am indebted to Dr. Louria for this opportunity and many others to see remarkable cases.

As you are probably aware, I have had the opportunity of pointing out and proving that many cases in which there must have been an infection of one or more valves of the heart by an anhemolytic streptococcus (or an influenza bacillus), the patients have become spontaneously free from the infection before coming under our observation. It seemed remarkable to find that people could come to us and present phenomena that had been put down as part of their valvular defect, and really be cases of streptococcus endocarditis in which the streptococci had spontaneously disap-

peared from the blood. Nearly all these cases have gone on to a fatal termination because of the after-results of the infection. Up to February, 1917, I had had the privilege of observing in the wards of the hospital 76 cases which I suspected of being in the bacterial stage of a subacute streptococcus endocarditis and in which the diagnosis was absolutely proved in 64. During the same period there were 33 cases suspected of being in the bacteria-free stage of subacute streptococcus endocarditis, in 20 of which the diagnosis was absolutely proved. If we take together the suspected cases in both groups 33 and 76, we find that at least one-third of the cases come to us in the bacteria-free stage. If, for the sake of greater accuracy, we take together the 20 proved cases in the bacteria-free stage and the 64 actually proved to be in the bacterial stage, we find that at least one-fourth of the cases come to the hospital spontaneously bacteria free. It is evident, therefore, that in cases in which there has been an infection of the valves of the heart by an anhemolytic streptococcus at least one-third to one-fourth spontaneously become rid of their infection. The figure must, however, be even larger than this. The cases in the active stage were studied by me through the kindness of the visiting physicians of the hospital in a number of the wards. The cases in the bacteria-free stage were nearly all observed on the service of my former chief, Dr. Rudisch, or on my own service. As there must have been a number of cases in the other wards which I did not have the time to follow up for any prolonged period (these cases require observation over very long periods, sometimes for several years), it is clear that the number of people who develop a streptococcus infection of the valve and spontaneously lose the infection is amazingly large. It will be very important to study, when possible, the process by which the bacteria are gotten rid of in such cases, in an attempt to obtain a better clue to the treatment.

I have seen a remarkable case of recurrent infection in a case of endocarditis in the bacteria-free stage. The diagnosis was established clinically. It must be left to future studies to determine how often such a recurrence takes place. I have been asked the question very often and have not been able to answer it.

In the preceding part of my remarks you may have noticed that I have not mentioned much the cases of the subacute type due to the influenza bacillus. As far as our studies up to the present time indicate, whatever holds true of the streptococcus cases holds generally true of the influenza bacillus cases. There is at least one clinical difference. The influenzal cases are characterized by a great tendency to develop a marked nephritis and to present marked clinical symptoms of the renal diseases. In cases of anhemolytic streptococcus infection it is very unusual for the renal disorder to make itself so conspicuous in the active stage. Renal symptoms are, however, frequent in the bacteria-free cases. The influenzal cases are so few in number that I prefer to call the disease as a whole "subacute streptococcus endocarditis." No great error is made in that way. It is important, however, in every case in which a streptococcus is not found in the blood to keep in mind the possibility that the case may be one due to the influenza bacillus. The latter is much more difficult to culture from the blood than the streptococcus, and for that reason, whenever a case that is suspected of being one of subacute endocarditis (chronic malignant endocarditis) and the blood-culture is negative, although the patient is febrile, particular pains should be taken to try to recover an influenza bacillus that may be present.

Apart from the verrucous type of endocarditis that is found in cases of infection by the rheumatic virus, there is another form of verrucous endocarditis that is usually called "terminal" or "cachectic." It occurs particularly in cases of diabetes, gout, carcinoma, tuberculosis, chronic cystitis, and old lesions of the nervous system. The lesions that have usually been described are similar to those in which the infection is rheumatic in origin. Bacteria, however, have only rarely been found in sections. When found, they were cocci.

These cases are to be sharply distinguished from cases of terminal bacterial endocarditis. In the latter the blood-culture is usually positive and the lesions are full of bacteria. The lesions are very small only because the patients die before they have a chance to develop to any considerable size. It is very important

that further studies be made not only as regards the etiology of this terminal verrucous endocarditis, but also as regards the histology. It has been suggested by Harbitz that they may be, at least at times, due to products of abnormal metabolism. It is important to study these lesions very accurately to determine whether there are differences between these lesions and those found in cases of rheumatic infection. In the non-rheumatic verrucous endocarditis cases Aschoff bodies are not present in the muscle of the heart. Aschoff bodies might not be present in a case of terminal rheumatic endocarditis because of the short duration of the disease.

Instances of tuberculous endocarditis have been described, but according to those who have studied the subject most the lesion is exceedingly rare. As mentioned above, a verrucous type of endocarditis can occur in cases of tuberculosis. In most of the instances in which this has been present the histologic changes have not been those of tuberculosis and tubercle bacilli have not been demonstrated.

An atherosclerosis in itself does not constitute a true endocarditis, because the lesion is not inflammatory but degenerative. The valvular defect resulting from such a process may become the seat of a bacterial infection. This occurs much less often than when the valvular defect is the result of rheumatic fever or syphilis, and the infection is more frequently of the acute variety.

Most of the bacterial infections are engrafted upon valves which have been damaged by the virus of rheumatism. The number of instances of valvular defects of rheumatic origin which later become the seat of non-rheumatic or non-syphilitic endocarditis is remarkably large compared to the number of instances in which this occurs on the basis of valvular defect due to lues, considering that lues is such a close second to rheumatism in causing valvular disease.

Finally, besides the forms of valvular conditions described above, there are some cases that we have not yet been able to classify. I have seen several cases with remarkably diffuse flat lesions either on the valve alone or extending over the endocardium of the walls of the heart in which no bacteria or spiro-

chetes could be found. Nor were there Aschoff bodies in the heart muscle or evidences of luetic infection in the blood. Furthermore, in some cases of mitral stenosis with a very dense fibrous valve, peculiar ulcerations with or without thrombotic deposits are sometimes found, the cause of which it is difficult to give. They appear at times to be caused by breaking down of tissue due to insufficient blood-supply, and at other times they resemble the peculiar clefts and ulcers of the valve which are found rarely as the only evidence of a previous subacute streptococcus endocarditis.

It is very important, as I have stated above, to keep in mind in making diagnoses the sharp distinction that must be made between a valvular defect and an endocarditis. The diagnosis of syphilitic diseases of a valve before the valvular defect is an accomplished fact I cannot discuss because of lack of sufficient studies on the subject. There is a sharp distinction clinically between the cases of rheumatic endocarditis and those due to the various bacteria which we have above named. In cases of rheumatic endocarditis the lesions are firm and small. It is doubtful if they ever break off, and if so, they are so small that they would not plug a vessel of any importance. In cases of endocarditis due to the bacteria which we have mentioned above the lesions are usually large and embolisms are of frequent occurrence. When present, they constitute a sharp differentiation from rheumatic endocarditis. My experience has been that we do not encounter embolisms which we can recognize in cases of valvular defect or cases of rheumatic endocarditis.

Of course it is possible for a person with a valvular defect (tight mitral stenosis) to develop a thrombosis in the auricle and get an embolism from that source. Or it may happen in a case of valvular defect or of rheumatic endocarditis that the patient may, because of cardiac weakness, develop a thrombosis in the ventricle and develop an embolism from that source. It can also occur that the patient has a thrombus in one of the peripheral veins and develops a paradoxic embolism by way of a congenital cardiac defect. Or, finally, there may be a thrombus on an ulcerated patch of the aorta or one of its branches or a

thrombus in one of the pulmonary veins (these thromboses, of course, are not infrequently present in various types of lung disease, especially necrotic lesions), and from such thrombi embolisms may develop. These occurrences, however, are all very rare. The fact remains that when they are absent and an embolism is found in a case of valvular disease it means that that patient has more than a valvular defect and has more than a rheumatic endocarditis. It signifies that the patient has an endocarditis due to one of the known bacteria, and then it must be determined whether the patient is in the active or bacteria-free stage. What holds true for embolisms holds even more true for embolic aneurysms, because these are not produced by the various forms of thrombosis which I have mentioned above.

Several years ago, after I had begun to realize the importance of embolism in the differential diagnosis in cardiac disease, I had the opportunity of studying a case which was most instructive. The patient was a girl about eighteen years of age, who came into the hospital suffering from a mitral stenosis, and running an irregular temperature without chills. There were no petechiæ at any time nor any embolisms in the peripheral vessels. There were no inflamed joints, but there was a previous history of what was designated as rheumatic fever. After the patient was in the hospital several weeks she developed a hemiplegia.

Up to that time I had been in doubt as to whether the case was one of rheumatic infection of the valve or a case of subacute streptococcus or influenzal endocarditis in which the blood-cultures remained negative. The case had a type of fever which when present in cases of subacute bacterial endocarditis is usually accompanied by a positive blood-culture. As the blood-cultures were repeatedly negative, we leaned more to the diagnosis of a probable rheumatic endocarditis. We did not believe that the hemiplegia could be traced to a luetic infection of the brain because the Wassermann reaction was negative. I was asked by the interns whether the occurrence of the cerebral embolism did not preclude the diagnosis of a rheumatic endocarditis because I had made the statement that a true rheumatic endocarditis does not produce embolisms of clinical importance. I answered

that the case might still be one of rheumatic endocarditis and the embolism might be derived from a thrombus in the left auricle, a not infrequent occurrence, as you know, in late cases of mitral stenosis. At the postmortem examination there was found a thrombus in the left auricle. To make the demonstration more striking the verrucous endocarditis which we did find was not on the mitral valve, but on the tricuspid valve, from which site, of course, an embolism could not reach the brain. The heart muscle contained numerous Aschoff bodies. I shall at another time describe other illustrative cases.

If you have understood the statement I made today the terminology of the diseases of the valves of the heart becomes a more simple matter, and you will not say more than you know. If the patient has only the results of a previous infection or disease of the valve of the heart, that is a "valvular defect," and should not be called a chronic endocarditis. The term "chronic endocarditis" can be used only for cases of chronically recurrent syphilitic or rheumatic disease of the valves of the heart, and then the terms to be used are, according to which the case is, "chronic syphilitic endocarditis" or "chronic rheumatic endocarditis." However, as I have told you, it is very difficult to say that the case is one of chronic syphilitic endocarditis. Such a diagnosis could only be made if the patient had a valvular defect, kept on having fever or other evidences of active infection, kept on having a positive Wassermann, and you could exclude any other kind of infection of the valve.

Whether a real chronic rheumatic endocarditis occurs I do not know. We shall probably learn that it is better to call such cases "valvular defect with recurrent rheumatic endocarditis."

The cases of endocarditis definitely due to bacteria should be called according to the name of the infecting organism and the course of the disease, the necessity for which nomenclature I emphasized in an address given before the Johns Hopkins Medical School in 1906. Thus a case of endocarditis with an acute course due to a hemolytic streptococcus would be called "acute streptococcus endocarditis." It is not necessary to add the word hemolytic, because the organism generally found in the

acute cases is hemolytic. Only if the case had an acute course and the streptococcus found was anhemolytic we would, so as to be precise, call the case "acute streptococcus (anhemolytic) endocarditis," or still better, "acute anhemolytic streptococcus endocarditis."

Similarly, if a case be one of subacute course due to the influenza bacillus, we would call the case "subacute influenzal endocarditis." If the case should run a subacute course and be due to an anhemolytic streptococcus, the case should be called "subacute streptococcus endocarditis" because we know that the organism found in the subacute cases is practically always the anhemolytic streptococcus, and never a hemolytic streptococcus. If the patient has a previous valvular lesion and has an endocarditis of acute type due to streptococci, the diagnosis should be "valvular defect with acute streptococcus endocarditis." If the valvular defect should be due to syphilis some might wish to add that term and say, "syphilitic valvular defect with acute streptococcus endocarditis."

The terms "acute" and "subacute" when applied to endocarditis are not simply of importance as regards the duration of the disease. In the subacute type of the disease, whether due to the streptococcus or due to the influenza bacillus, there are clinical phenomena and lesions which are absent in the acute types of the disease. For instance, the tender cutaneous embolic nodules occur only in endocarditis cases with a subacute course. Their presence in a case at once convinces us that if the case is still in the bacterial stage we are almost sure to find in the blood an anhemolytic streptococcus or, rarely, the influenza bacillus. Similarly in the kidneys there are embolic lesions of the glomeruli, as you know, which occur only in the subacute cases, whether they are due to the streptococcus or the influenza bacillus. Other differential features I shall take up when I discuss with you on a later occasion the clinical features of these various forms of endocarditis.

CLINIC OF DR. HARLOW BROOKS

UNIVERSITY AND BELLEVUE HOSPITAL MEDICAL COLLEGE,
CITY HOSPITAL

A CASE OF COMBINED CHLORIN GAS AND TRINITRO-TOLUENE POISONING

THIS patient has just been sent up from the dispensary, and since he appears to illustrate a very interesting and, at the present time, particularly pertinent condition, I have decided to present him before you even in this but very hastily prepared state, and especially since from his general appearance it seems quite probable that we shall be unable to present him to you later.

As he enters the room you notice his very marked dyspnea, and the striking color of the exposed portions of the body, the face, neck, and hands. It is a curious combination of the blue of cyanosis with the yellow of a marked jaundice, mingled with such a gray shade as we see in cases of *extremis*.

I shall not ask him to lie down on the examining table for the present, for the prone posture greatly intensifies his dyspnea. As he sits down in the chair you note how he throws his shoulders forward and bends the thorax anteriorly, as does a sufferer from an attack of bronchial asthma. I do not need to ask you if this patient is really sick, or if he is a malingerer, yet in this condition he has traveled in the trolleys a considerable distance from a Long Island suburb to our dispensary.

As we remove his clothing you note the magnificently formed shoulders and back, the perfectly and massively turned muscles, and the well-nourished trunk. It is apparent, then, that this patient is suffering from a relatively acute condition and one which has as yet not greatly exhausted him. He is 71 inches in height and weighs probably at least 180 pounds, as you see he

is throughout beautifully proportioned. His skin is universally of the peculiar hue which we noted as he entered the room, but the eyes are not much bile stained, as you see. His breathing is very labored, though it is somewhat easier now that he has been seated for a moment.

Dr. Brooks: As the patient now appears to you, do you consider him in a grave condition, and what type of disease is first suggested to you?

A Student: He certainly is seriously ill, and he looks like a man suffering from cardiac dilatation with jaundice.

Dr. Brooks: But the pulse is full and strong, rate 72, counted at the apex; there is no arhythmia; there is, as you see, no edema of the ankles, face, or hands. He is jaundiced and quite deeply so, the urine contains large amounts of bile, but note that the conjunctivæ are but slightly stained.

Student: Perhaps he has a pneumonia or some obstruction in his bronchi.

Dr. Brooks: His dry, distressing cough might further suggest some such condition, but he has a slow pulse and his rectal temperature, as it was taken in the dispensary a few moments ago, was but 99.5° F. He is not in collapse as afebrile cases of pneumonia would be, and though (as one of you I see is suggesting) the slow pulse may be due to the jaundice, it is quite certain also that he is not suffering from an ordinary pneumonia after the crisis. Will one of the young gentlemen please come down into the amphitheater and examine this patient's hands?

Student: The palms are stained bright yellow.

Dr. Brooks: Is it the yellow of the jaundice or perhaps that of cigarette stains?

Student: It can be neither of these, for it is a bright yellow like a nitric acid stain; it is diffused all over the palms, and they appear in places to be bruised and inflamed; the lesions suggest burns. It must have something to do with his occupation.

Dr. Brooks: Smell of his hands.

Student: His hands smell as does his breath, only much less so. The odor is like that of strong chlorid of lime.

Dr. Brooks: Now you young gentlemen of the front seats have discovered the source of the strong odor of chlorin, rather more as your colleague says that of chlorid of lime which pervades the room, and I imagine that this odor can be detected even well up in the ampitheater.

Students: It can.

Dr. Brooks: Now I shall give you the history and such of the physical findings as we have been able to make out in the dispensary.

He is twenty-seven years old, recently married, no children. Born of Polish parents in New York, where he has always lived. His previous history is of very little importance, but he comes of a vigorous stock and has been a common laborer of great strength and little sickness up to five months ago. He denies having had any of the venereal infections. Physical examinations thus far substantiate this statement. He insists that he has always been perfectly well up to five months ago, when because of the high pay offered he entered a chemical factory engaged in the manufacture of explosives. I shall tell you of the process as the patient has told it to me, and if I err, the patient, who is a man of more than ordinary intelligence, will correct me, for as you see, now that he has remained seated for this time, he is able to talk with reasonable comfort. I am entirely unfamiliar with this process myself, and, indeed, except in a very crude way with the chemicals employed, except that picric acid or its compounds I know is not used or manufactured in this plant. It may well be therefore that the names employed for the materials used are incorrect. I believe that the process practised in this as in many similar plants is more or less secret, and it is more than probable that the workmen are poorly or entirely incorrectly informed as to the material with which they work.

The patient was working in the "chlorin shed"; 25 pounds of toluol is given to each workman, it is placed in a bottle, and to this mixture $\frac{1}{4}$ pound of "phosphate of trichlorid" is added and shaken up with the mixture, which is then emptied into a receptacle through which chlorin gas is run. A considerable amount of leakage of gas takes place through the connections of rubber

and glass, and the patient states that a degree of protection from the disagreeable fumes is provided by the issue by the Company of gas masks. He, however, states that these masks are "no good"; that they are uncomfortable and a nuisance to rapid work; I gather that they are not worn with any very great regularity; the patient, as his smile indicates, does not disagree with this supposition. The perfusion of chlorin gas continues until the mixture reaches a specific gravity of 1.031, when it is mixed in a galvanized drum and then emptied into a carboy. Just what the resulting mixture is neither the patient nor I know. The respirators are supposed to be kept moistened with sodium bicarbonate, but the fumes of the gas penetrate nevertheless. Presumably, then, the gas was at least an acid one, and if we may judge from the patient's breath, which he insists is like that of the fumes in the mixing-room, certainly at least it is some loose combination of chlorin.

Part of the time the patient also handles trinitrotoluol, usually with the bare hands, though the workmen are urged to use rubber gloves, but as the company refused to provide these, urging the men to be careful not to stain the hands with this chemical, which, as you probably know, is quite poisonous and may be taken up by the lymphatics, many of the men, as was the case with our patient, usually neglected this formality.

Most of the men engaged in this manufacture, the patient states, sooner or later began to suffer from the effects of the chemicals, and three weeks before he came to Dr. Carroll in the dispensary the patient began to note, first, that he vomited persistently before, after, and often between meals. No real nausea, as a rule, preceded the vomiting. He also began to have with increasing intensity intervals of severe knife-like abdominal pains. He now noted the presence of occasional blood in the stools. The bowels move usually twice or more daily, but no real diarrhea has appeared. The vomitus, he notes, consists usually of the partly digested food mingled with much yellow mucus; bright blood was also often present, especially at those times when he appeared to have inhaled more of the irritating fumes.

He has also suffered much from severe headache of a generalized character, bursting and throbbing in character and accompanied by vertigo and much dizziness. As he has detailed these symptoms to me they strongly suggest the headache which follows the administration of powerful doses of the nitrites, of amyl nitrite, for example.

His eyesight has become very defective; when he closes the eyes he sees black spots floating before him, and on opening them the spots still appear, but they are now white and nebulous. He has noted tingling and numbness in the hands and feet, his station and gait have become uncertain. He has noticed the slight jaundice of his sclera and more of the skin. All the men get it sooner or later he says, but there has been no pruritus, no insane desire to scratch.

A cough has developed, and has now become, as you see, of a very insistent character. It results now in the expectoration of a heavy whitish sputum which at times contains black or brown material, looking like broken-down blood. It has the intense chlorin odor as demonstrated in the specimen which I present for your inspection. Note that the odor is purely that of the chlorin; there is no putrid or sweetish odor. It may be, of course, that any such might be overdominated by the chemical smell.

He has become, as you note from his voice, very hoarse, the throat has become very sore and dry, his nasal mucosæ are in a like condition, as you will note on inspection. Everything that he eats has the sickening taste of chlorin.

He suffers greatly from dyspnea, and as you noted when he entered the clinic this is very much accentuated by the slightest exercise or by the prone posture. He has a gripping, grinding sense of oppression and pain in the precordium, also much exaggerated by slight exercise. He believes that his heart palpitates violently at times. This we have not yet observed. He says that pain radiates down the arms from the precordial region, more so on the left. About two months ago he noticed a little swelling of the ankles; it is now much less or absent.

His appetite is very poor, he sleeps very badly, and his rest is

disturbed by outrageous dreams and fancies. Sexual desire has gone; he has become very weak generally. His weight has fallen from 197 pounds four months ago to 175 pounds today. He does not complain of polyuria or of nocturia, but at times he has difficulty in starting the flow, and it dribbles after he attempts to check it.

Three days ago he stopped work because he was laid off the shift, but he confesses that he does not feel well enough to work now, and he quaintly admits that he has been worse since he stopped work. Indeed, in this condition maximum symptoms do not appear at once.

His habits appear to have been fairly good, he takes about one glass of beer and perhaps one of whisky daily, never cared much for it, but he does smoke about one package of cigarettes daily. He could not smoke during his working hours because of a factory rule.

Five days ago he was prostrated by a sudden attack of suffocation, during which he became unconscious for about twenty minutes.

His chief complaints are dyspnea, precordial pain, weakness, persistent cough, headache, and failing eyesight. His mentality appears to be quite normal, his general viewpoint appears to rather diminish than to exaggerate his symptoms.

We will ask him to lie down on the table for more satisfactory examination. You note at once how much more difficult his breathing becomes and how his cyanosis deepens; his skin is covered now by a cold sweat. As we bolster his head and thorax up, note that considerable relief follows, but still the respiratory movements are very forced, he is suffering, struggling for breath, and his facial expression portrays his agony better than his words might.

I am unable to make out the borders of the heart, due largely to the fact apparently that there appears to be flattened percussion over the adjacent lungs. The use of the tuning-fork and of auscultatory percusson does not help in this respect. The heart action is slow, the muscle tone booming and clean. I fail to discover any murmurs; every ventricular beat comes through to

the radials in regular, strong, and even pulsation. The veins of his neck are distended, however, and he seems to obtain some relief from the dyspnea by raising his arms with his hands folded over the vertex, the muscles fixed. The superficial vessels are not palpably diseased. The fault, then, does not appear to be a circulatory one.

As I auscultate the lung areas I find curious districts of lost breath sounds very irregularly distributed, silent areas over which fremitus is much diminished and the percussion-note high pitched and flattened. These areas are, as you see, indicated by the pencil-marks, some at the base, laterally, some in the upper lobes. They are as clearly defined as a disseminated neoplasm of the lung and between these areas the breath sounds are exaggerated. Both expiration and inspiration are accompanied by bubbling and musical râles. In such places as I show you here the percussion-note is almost as clear and booming as the voice of an old-fashioned tenor drum, it is almost bell-like.

Coughing and expectoration cause marvelous changes in the breath sounds, in some places they become almost amphoric. Still the silent areas persist, change in posture does not affect them, apparently they are fixed. Their location, wide dissemination, and isolation show us that it is not due to pleural fluid nor apparently to patches of pleural thickening. I have never seen a condition in which such silent areas were so definite and marked except in disseminated pulmonary neoplasm.

The abdomen is stiff and rigid, yet I palpate the lower border of the liver apparently with ease; it is smooth, lies fully a handbreadth below the arch, and even such gentle pressure as I use in this palpitation causes the patient to wince; it must be exquisitely tender, I can feel no nodules and no areas of special tenderness, the liver does not pulsate, and there are no adventitious sounds to be heard over it on auscultation. I cannot make out the splenic dulness even by auscultatory percussion; the abdomen is too stiff certainly for me to expect to be able to feel other than a greatly enlarged spleen; this is not present. The percussion-note over the colon is tympanitic; on auscultation over the caput I hear the gurgling as from the passage of much gas.

The tongue is large, soft, tremulous, and gray. The pharynx and the mucosa of the nose as well is red, eroded, dry, and streaked by shreds of tenacious mucus. Some of the capillaries are eroded and show small bleeding points. My examination of the larynx is not very satisfactory, due to these paroxysms of cough, but its mucosa seems to be like that of the upper membranes.

The facial expression is that of suffering. The pupils are widely dilated, they react to light and accommodation very slowly and incompletely. Even in the dim but unsatisfactory light of the amphitheater I am able to make out with the ophthalmoscope that the optic nerve in both eyes is pearly white; it is swollen and bulges over like a fresh mushroom. Many pearly white patches of degeneration are diffusely scattered over both retinæ and both show hemorrhages mostly quite recent. There appears to be no definite distribution of these striking lesions. I have seen such changes in very advanced albuminuric retinitis, but we must refer this matter to the ophthalmologists.

The thyroid appears to be prominent, the muscles of the neck are rigid and beautifully demonstrated, the veins swollen.

There appears to be little or no edema of the ankles or wrists and the extremities, aside from the universal jaundice, seem to be in normal condition. Crude sensory tests such as we are employing indicate no gross sensory defects. The knee-jerks are active and about equal. There is no Kernig, no Babinski, no Oppenheim, no clonus. It seems thus far that the cord and brain have escaped then. The peculiar orange coloration of the palms is due to the handling of the toluol, is it not?

PATIENT: Most of us get that, you can't wash it off.

DR. BROOKS: Dr Alice Hamilton in a recent report of trinitrotoluene poisoning mentions the fact that the pigment stains enter the deeper layers of the skin.

The emergency laboratory tests made in the dispensary show the casual specimen of urine to contain a large amount of albumin, much bile, and no sugar. Specific gravity 1.025. The hemoglobin is 75 per cent. The blood-pressure shows systolic 160 mm. Hg., diastolic 90 mm.

Before we go any farther into the discussion of this rather unusual case, I think that you will all agree with Dr. Carroll that he should be taken at once to the hospital—this is hardly a case for dispensary treatment. I shall not fail to keep you informed as to the progress of the case. (Patient leaves room.)

This case presents a quite unusual condition of affairs. Our lack of definite technical knowledge of the processes of manufacture in which this man is engaged hamper us very much in our discussion of the case, but it seems to me that we have, however, more than a single factor to consider in the etiology. The patient has been confessedly carelessly handling at least two very poisonous substances of which we know at least a little. The dominant picture is that of respiratory embarrassment, and we find in his lungs and in the upper respiratory passages as well conditions of the utmost importance, but which admit of several possibilities in the way of explanation.

He has been constantly working in an atmosphere laden with chlorin gas. All of us know to a certain extent at least what the effects of the inhalation of chlorin gas are—to a considerable degree they are similar to the inhalation of the fumes of nitric acid, and it is quite possible that the nitric fumes may be also concerned in this case, for they are much employed in the manufacture of the modern explosives. Lehman has shown experimentally that the inhalation of chlorin and bromin fumes induce practically identical lung lesions—emphysema from the violence of the coughing paroxysms, purulent bronchitis, and bronchopneumonia. James Ewing several years ago pointed out to me lesions of this same character in the lungs of a person who died from the effects of the inhalation of the fumes of a supposed nitric acid compound in which a necrosis of the mucous membrane of the walls of the bronchi had taken place apparently with a coagulative process. As a result of this bronchial obliteration patches of microscopic atelectasis had developed within the lung, alternating with areas of emphysema, the atelectasis, of course, resulting from the plugging of the bronchioles. Subsequently bronchopneumonia is to be expected. This does not as yet seem to have taken place, for the patient has neither rapid pulse nor temperature. I expect,

however, that this will take place if the patient survives sufficiently long, which I much doubt.

In the literature of the subject I do not recall an instance in which the distinct odor of the chlorin was so long preserved or so very definite as in this case. It seems to me probable that the chlorin may have entered into a loose combination with the necrotic tissue of the bronchial walls and with the mucus, and may be thus longer retained.

I am then inclined to explain these remarkable silent areas in the lung in this case by the assumption that the inhalation of the chlorin gas has caused a necrotic bronchitis, and that a resulting plugging of the bronchioles has been followed by remarkable islands of atelectasis. Of course, we must not be so carried away by the chlorin theory that we forget the possibility of a disseminated pulmonary tuberculosis or of pulmonary neoplasm. Time and the fluoroscope should, however, clear up these points for us if the pathologist does not.

Changes like these, both postmortem, and symptoms like these clinically have recently been extensively reported from the war hospitals as a result of "gassing." Friends serving with the medical departments of our allies report to me very similar findings, many of them, as in this case, unaccompanied by temperature, and in which the atelectasis is followed by a fibrosis even without a true bronchopneumonia developing. The recent journals devoted to military medicine have made us familiar with the very serious effects of these irritant gases. It is very probable that many of us will soon become personally acquainted with such effects of German "Kultur."

Such a theory of patches of atelectasis following the fibrinous bronchitis which we then know follows chlorin or other irritant gas poisoning readily explains the signs of respiratory distress, but it does not help us out in the explanation of the jaundce, of the large and very tender liver, of the albuminuria, and of the remarkable changes in the eye-grounds. In none of the literature of the subject with which I am acquainted are such findings reported, nor can I understand their occurrence from what we know of the action of chlorin gas.

In the manufacture of the more recent explosives chemical compounds allied to the analins, for example, nitrobenzine, which is used in the manufacture of anelin, and probably similar materials used in the manipulation of toloul, produce toxic symptoms suggestively like some of those in our case.

Taylor gives as the symptoms of anelin poisoning, cyanosis, coma, and vomiting. Pockley reports the case of a mixer of roburite (roburite is one of the newer explosives into which the anelin substances largely enter) in which failure of sight, dyspnea, cyanosis, and vertigo appeared. Changes in the retinæ are also reported from this cause. But for a more satisfactory explanation of the signs evidenced in this case we must have recourse to more recent literature, and notably to the very important communication of Martland, of Newark, one of our old City Hospital men, by the way. Martland, from the pathologic study of cases of trinitrotoluol cases, particularly draws attention to a remarkable degenerative change which appears in the liver leading to extensive necrosis, which produces marked jaundice, degeneration of the kidney parenchyma, and cloudy swelling of the heart muscle, which from his description appear to be very similar to the changes probably responsible for the patient which we have seen today. John Larkin, from his wide experience with cases of this kind at autopsy, corroborates Martland's findings. In discussing the matter with Dr. Clark, of Lynhurst, who has medical charge of a large munition plant in which trinitrotoluol is extensively employed, I find that such a picture as our patient today presents is the frequent result of poisoning with this drug, corroborating also the statements of Alice Hamilton, who apparently was among the first to study this form of occupational disease in America. She has collected upward of 700 cases.

It appears to me, however, that the case which we have just seen presents a definite combination of a chlorin poisoning with a trinitrotoluol toxemia. This man is virtually a "gassed" patient, who has, in addition, extensive degenerative changes in the liver, kidney, and eye-grounds due doubtless to this form of explosive, that is, to the toluol compound.

As to the prognosis. Experience with those who have suffered

from chlorin poisoning alone, even when slight, is not favorable, more or less bronchopneumonia nearly always appears, and a chronic bronchitis with pulmonary fibrosis is to be expected. In this case we have added the grave liver, renal, and deep ganglionic cell degenerations due to the other toxin. It seems obvious that our prognosis must be very bad.

In the way of treatment we shall, of course, put the patient to bed, though with the back-rest, for it is unlikely that he will be able to lie down flat. I shall attempt to mitigate the exhaustion of this racking cough by the use of codein or morphin in as small doses as the control of the symptom will permit. He will be thoroughly cleared out by the administration of magnesium sulphate and his diet will be fluid and very low in calories. Probably for the first twenty-four hours he will receive but 32 ounces of milk, but, unlike the procedure in the usual Karell diet, we shall not only allow but shall encourage the taking of fluid, that is, of distilled water. Perhaps later, depending on whether or not sugar is present in the urine, that is, whether the pancreas is or is not competant, we may give him the lactose orangeade of which I have spoken to you rather frequently. In other words, diet him as we would a case of acute nephritis, always, of course, trying to keep our chlorin intake low, so that the tissues may more readily free themselves from the excessive chlorids now probably present in them.

Nineteen Days Later.—Young gentlemen, you will recall my showing you nineteen days ago in this clinic a case of combined chlorin and trinitrotoluol poisoning. You will recall, I am certain, the general features of the case and the very desperate condition in which he appeared to be. You remember that I gave a very gloomy prognosis and perhaps there are those among you who felt that I should have reported the autopsy findings to you before now. He discharged himself from the hospital today in such condition that he stated that he wished to return at once to work, though not again to the munition factory.

Almost with the hour of his entrance to the hospital he began to improve. Inside of three days from the time of entrance the cough was well under control, the cyanosis had much diminished,

and inside of a week the jaundice had disappeared. The tenderness and the swelling of the liver rapidly decreased and today we found the lower border of the liver but a little below the costal arch. The strong odor of chlorin was absent after five days, though the sputum was very rich in chlorids for a longer period.

Albumin rapidly disappeared from the urine, as did also the bile. No sugar or casts were present, but at first and quite naturally the amount of chlorids was greatly increased; this also rapidly righted itself.

You remember the very curious areas of silence over the lung. *x*-Ray plates tend to verify our diagnosis of isolated areas of atelectasis, and by the same means a dilatation of the right heart was made out. This soon corrected itself.

Quite contrary to my expectations, numerous blood examinations even when the patient first entered my ward showed surprisingly few changes. The Hb. was 75 per cent., R. B. C. 7,200,000, W. B. C. 9000, with a differential count of polynuclears 76 per cent., S. lymphos. 18 per cent., L. lymphos. 2 per cent., Trans. 1 per cent., eosinophils 1 per cent. The high rc. count is, of course, about what was to be expected in a cyanosed case, but it is interesting to note that one of the Martland cases of trinitrotoluene poisoning showed a marked aplastic anemia.

Gastric analysis after a test-meal of tea and toast showed neither blood nor bile. Total acidity 60, free HCl 35. No lactic acid. Pepsin apparently in sufficient amounts. The Wassermann reaction was found to be negative. One day after his admission the carbon dioxid capacity of the blood-plasma by the Van Slyke method was found to be 48; certainly much better than his clinical aspect led us to expect.

The blood urea nitrogen was determined on two occasions, one early in the course of his stay in the hospital, the other shortly before his discharge; it showed on both occasions 6 mg. per 100 c.c. Blood uric acid, 1.9 mg. per 100 c.c. From the very outset he showed an excellent renal capacity, was able to concentrate, and the line of fluid intake was closely followed by that of urine output. His blood-pressure chart presented nothing of note,

and shortly after admission his T. P. R. ratio was absolutely normal.

Examination of the fundi by Dr. Gilfillan resulted in a diagnosis of bilateral retinitis and optic neuritis. One of the most remarkable features of the case, to my mind, was the very rapid clearing of the retinal lesions with commensurate improvement in the eyesight.

Of course the patient was by no means well when he left the hospital, and, of course, he left also against our advice, but his improvement has been so remarkable that it is difficult indeed to realize that it was possible. It perhaps may illustrate to us what experience teaches us daily—the great difficulty of prognosis. This has been no therapeutic achievement, this case has simply shown the sometimes remarkable ability of the body in youth and with previous health to rid itself o f even so very serious lesions as were doubtless present in this case. One further word about the pulmonary findings. The areas of absent breath sounds and of flattened percussion cleared up in part, but not entirely. Pulmonary symptoms largely disappeared, but the signs persisted, and I am strongly of the opinion that our patient will suffer from these lesions in the future. In my opinion chronic bronchitis and eventual pulmonary fibrosis are inevitable. At the last, however, the scanty sputum showed little suggestive of disease.

Our diagnosis has probably been verified, but our immediate prognosis has been most happily disproved. I have not discussed our treatment more fully because apparently the case recovered of its own energy instead of because of his treatment.

ACUTE HEART-BLOCK DUE TO SYPHILIS

WHEN we were discussing the subject of heart-block some time ago you will recall that I made the statement that occasionally this clinical picture developed very acutely and in altogether unexpected cases. A beautiful example of this kind has been generously referred to me by our greatly esteemed colleague, Emanuel Libman, who, knowing of my interest in this subject, kindly sent the case to me.

The patient is a well-built man of thirty-one years. By occupation he is a distiller of whisky; the patient naively adds, "Also consumer of the same." As a child he was inclined to precocity mentally, but has always been physically indolent except in certain traits, to be presently suggested. He suffered from most of the diseases of childhood, including measles of both varieties, scarlet fever, and mumps. Owing to his wilful nature and winning ways his diet from early childhood has been most inadvisedly chosen. He has been an overly petted and favorite son of a very lovely and indulgent mother.

In early youth he began to suffer from gonorrhea, of which he thinks he has had seven or eight distinct attacks; he is rather undecided as to the precise number, but it is quite certain that he has never permitted himself to become sufficiently cured before re-exposure in any instance to be at all certain whether or not he has ever completely recovered from his first infection. He is still under sporadic treatment for chronic gonorrhea.

He denies having knowingly had syphilis, nor does he give a history of suspicious genital sore, skin rash, falling hair, persistent sore throat, or other hall-mark of this infection.

From early youth he has been an inveterate user of excessive numbers of cigarettes. He has been a generous consumer of alcoholics in all forms, preferring, however, his own product—whisky. He has on several occasions temporarily deserted his

regular occupation for that of financier, good angel, and chaperone of various theatrical ventures. He is welcomed at the stage door of most of the theaters of the more popular class devoted largely to the entertainment of the tired business man.

Apparently he has never had acute rheumatic fever, but he does give a history of having had tonsillitis three or four times, but never very severely. In fact, except for his history of excesses in almost every undesirable direction, he appears to have been very litttle ill, save, of course, for the chronic gonorrhea. He has never been fond of athletics, though naturally an excellent dancer. He has never chronically attended school, but is a most fascinating and persuasive young gentleman, with friends of both sexes in abundance. He has not been poverty stricken except for occasional acute outbreaks, exhibited for disciplinary purposes.

For eight months he has been suffering from sudden attacks of severe pain in the region of the precordium, associated at times with rapid loss of consciousness, though the attacks last but a few seconds at a time, probably not above thirty seconds. These attacks are becoming now more frequent, and they appear to be excited by physical effort, by emotional stress, and they occasionally appear unexpectedly, even when lying down and without any obvious reason. He had one of his worst attacks on the way to the city while mounting the stair leading from the dining saloon of the steamer on which he came. During this attack, which was inaugurated by a sense of oppression, then of pain in the region of the heart, with faintness, complete oblivion took place for a few instants, during which he clung to the rail of the gangway. He did not fall, but his face became deathly pale, and, as customary, the return to consciousness was accompanied by a tumultuous sensation in the precordium, some dyspnea, throbbing of the blood-vessels, and then he felt entirely normal. He was sent North, referred to Dr. Libman, with a diagnosis of epilepsy. After Dr. Libman had examined him and conducted certain tests, knowing of my particular interest in this condition, he generously turned the patient over to me for observation and treatment.

Physical Examination.—The patient is splendidly proportioned, 5 feet 11 inches in height, weight about 165 pounds. His musculature is, however, soft, not firm, nor of really sufficient volume for a man of his years and apparent vigor. His skin throughout is soft, devoid of scars, and of an entirely healthy texture. There are no skeletal defects demonstrable, the tibial borders are smooth, in no way roughened. There are no joint defects. The genitalia are normal and are apparently devoid of any scar.

The head, face, eyes, and ears are normal, but the tongue is large, soft, and flabby, its superior surface is ridged and grooved, certain areas bleed under slight provocation, palpitation of the tongue shows many areas of induration. There is just about one guess as to what this tongue suggests—that is, syphilis. The teeth are in poor condition; there is an extensive though well-cared for pyorrhea alveolaris. He has lost a good many teeth and has had extensive dental repairs of a high character of workmanship.

The neck is characterized by a rather prominent thyroid gland, and the lymph-nodes of the neck are evenly, though but moderately, enlarged. There is, however, no general lymphadenitis, no enlargement of the cuboidal nodes being particularly noted.

Examination of the lungs, larynx, and of the upper air-passages disclosed no lesion of note, though the tonsils are ragged, chronically inflamed, and the entire pharyngeal mucosa is congested, as one would expect to be the case in a chronic abuser of tobacco. There is nothing outside of the tongue which would suggest syphilis to me.

The pulse-rate varies from 58 to 68 per minute (seated). The pulse is full and regular, nothing suggestive in its palpitation except that it is somewhat slower than is usually the case in a young man of this clearly emotional type.

The cardiac outline, by percussion and auscultatory percussion, is M.R. 3.5 cm., M.L. 8 cm., B. 5 cm. These findings were subsequently substantially verified with the orthodiascope. The heart is in no way enlarged nor altered in its contour, in so

far as physical signs or fluoroscopy can determine. Careful examination often repeated at the usual areas showed absolutely no adventitious or otherwise abnormal sounds, and in this respect also nothing was to be made out. After thirty seconds of "double time," however, his pulse-rate fell to 40, counted by auscultation at the apex. No murmurs were to be made out, but the quality of the muscle tone was very uncertain and inconstant, and the pulse was not entirely regular. This condition soon passed away, but could always be excited by exercise. It was not tried many times, as you can well imagine, but during this period of slow pulse he became pale, faint, sweat and an expression of agony would appear on the face, and he complained of his familiar sensation already described. His appearance was not in the least such as to encourage further experiment. Examination of the superficial blood-vessels and of those of the retina showed no evidence of disease.

At the first examination the systolic blood-pressure was 130 mm. Hg., diastolic 88 mm. Subsequent determinations gave practically identical results. The hemoglobin was 77 per cent. No leukocyte or differential leukocyte counts were, I regret to confess, made. The Wassermann test gave a prompt report of 4 +.

Examination of the abdomen showed absolutely no demonstrable lesions. Frequent examinations of the urine, aside from the constant presence of shreds and of pus corpuscles with other evidences of chronic prostatic inflammation, were normal.

The knee-jerks were found to be considerably hyperactive, but no abnormal reflexes were present, nor was any abnormal cerebration evidenced, unless the patient's general attitude toward life as a whole may be considered in itself an indication of abnormality in this direction.

Taking the case as a whole we feel justified in the diagnosis of a syphilitic process, probably of a simple infiltratory character, chiefly if not exclusively involving the bundle of His. In other words, an acute heart-block incompletely established and of probable syphilitic origin.

Because of the lack of genital signs, of inguinal enlargement

other than that accounted for by the persistent gonorrhea, and of the very characteristic syphilitic lesions of the tongue, the likelihood of a primary lingual inoculation seems probable.

The condition of the patient appeared so serious to us that much as we desired it, to complete diagnosis, it was not deemed advisable to submit the patient to the strain of transportation to an electrocardiographic laboratory at the time, and he was at once ordered to bed and under the care of a competent nurse. All physical exercise was absolutely interdicted, alcoholics were forbidden, and the use of tobacco also denied. It is certain, however, that from time to time he did smoke a few cigatettes, though the danger of this was fully pointed out to him. Later on in his treatment he was allowed up to as many as ten cigarettes daily, which was less than one-fourth of his custom, but with the distinct understanding that he resumed smoking at his own risk and peril.

Because of certain unfortunate experiences of mine in the use of salvarsan in cases of heart-block in active syphilis I determined to withhold this drug until the patient had been fully brought under the effect of mercury. Because also of our firm conviction that we were dealing with a syphilitic process only, apparently corroborated by the normal heart outline and action when at rest, we gave him no digitalis, atropin, nor other form of cardiac stimulation.

He was given at once 1.5 gr. of mercury salicylate by intramuscular injection. Two days later his breath showed the characteristic odor of mercury and his gums were found to be slightly tender; nevertheless he was given 1 grain of the salicylate of mercury, when very definite salivation and mercurial gingivitis developed. Subsequently the salicylate of mercury was given in as large doses as possible, the attempt being made to keep just short of actual salivation. Of course the usual methods were employed to mitigate this, mouth-washes, the constant use of small doses of the saline cathartics, etc. After he had been under this vigorous mercurial treatment eleven days he obtained and drank a considerable amount of whisky, but apparently without ill effect. Without permission he got out of bed and walked

about the room without any discomfort, and it was now felt that salvarsan could be safely given. Twelve days after the beginning of treatment he was accordingly given 0.6 gm. of old salvarsan. He developed a temperature of 100° F. by mouth, a pulse-rate of 100, but without any signs of cardiac disturbance. The intramuscular injections of mercury were continued as before, and the pulse-rate now averaged in the prone position about 68 per minute, full and strong, and auscultation of the heart gave no evidences of disease. He was now officially allowed out of bed.

Further doses of salvarsan were refused because he began drinking in considerable quantities, smoking excessively, and he indulged at times in intercourse, all without apparent cardiac embarrassment.

Forty-two days after the first mercury injection he was discharged from my care and referred to the service of a syphilographer, since at this time no evidences of cardiac disease could be made out and electrocardiographic studies demonstrated an apparently normal acting heart in all respects.

I am, of course, not unmindful of the possibility of a tobacco angina in the case, but were this the condition it is practically certain that the quite typical Stokes-Adams syndrome would have reappeared when he again began his abuse of tobacco, alcohol, and of women.

When I last heard from this young man he was under active antisyphilitic medication, but he absolutely refused to discontinue his excesses, yet not the slightest indication of cardiac disease was present. Of course in a patient of this irrepressible type it is too much to expect that a complete cure of his lues will occur, certainly it is altogether undeserved, but I feel that the course of the case under treatment and typical signs and symptoms at the outset fully justify us in the diagnosis of an acute heart-block due to syphilitic invasion of the bundle of His.

CLINIC OF DR. ARTHUR F. CHACE

POSTGRADUATE MEDICAL SCHOOL AND HOSPITAL

DIET IN INTERSTITIAL NEPHRITIS

Demonstration of Different Forms of Diet. Possibilities in New Methods of Chemical Research. Parenchymatous Nephritis or Nephrosis. Retention of Water and Salt. Interstitial Nephritis. Uric Acid, Urea, and Creatinin. Importance of Low Protein Diet, Adequate Calories, Proper Balance of Amino-acids, Sufficient Mineral Salts (Particularly Iron), Presence of Food Accessories (Antiscorbutic and Vitamins). Illustrated by Charts of Sample Diets, Results of Chemical Examinations of the Blood Showing Effects of These Diets, Relative Food Values, Etc.

June 5, 1917.

THE subject of nephritis has so many ramifications that a discussion of it from every angle—the pathology, diagnosis, clinical observations, differential diagnosis, different forms, complications, prognosis, and methods of treatment—cannot be covered in one lecture. So I shall confine my talk today to the dietetic treatment of the interstitial form of the disease.

These trays do not mean that we are going to have luncheon here. It is an exhibition of low protein diets for nephritics, each one represented by the actual food in the individual trays in the exact amount to be taken with each meal. In this way you can visualize the diets and get an idea of how a gram bulks up.

(Here a survey was made of trays containing the foods which compose the diets outlined in Chart I, page 612. The weights and proportions were maintained and the appearance of the food made as attractive as possible.)

CHART I

Low Protein Diets for Nephritics

I. The juice from one lemon.
Two-thirds cup of water.
One tablespoon cane-sugar.
Six tablespoons lactose.
Serve four times a day.
For the day this gives 1242 calories, approximately 0.8 mg. iron and an alk. ash.

II. Morning and evening 300 grams of *ripe* bananas and 100 c.c. cream.
At noon 200 c.c. plain cream soup, 300 grams banana, and 200 c.c. milk.
(Cream soup consisting of 4 c.c. milk, 2.5 tbsp. flour, 2 tbsp. butter.)
For the day, 1335 calories, 29 gm. protein, alk. ash.

III. The lists I and II may be used advantageously in very severe cases in order given. Subsequent diets can be constructed from the following outline:

Morning.	*Noon.*	*Evening.*
Citrus fruit.	Cream Soup:	Rice:
Cereal:	Plain, asparagus, rice, celery, spinach, potato.	Steamed and cream.
Farina or		Steamed and baked banana.
Oatmeal.	Chief vegetables:	Pudding (20 gr., 4 c.c. milk, ⅓ c.c. sugar, 10 raisins).
Banana.	White potato, baked or boiled, baked sweet potato, banana.	Fruit:
Cream.		Ripe banana or stewed apple, prunes, apricot, peach, etc.
Toast.	Green vegetables:	
Beverage.	Asparagus, cauliflower, spinach, string beans.	Milk, 200 c.c.
	Lettuce salad with oil.	
	Cocoa (½ milk, ½ water).	
III*a*.		
Wheatena, 150 gm.	Cream of celery soup, 200 c.c.	Banana, 400 gm.
Banana, 200 gm.	Baked potato, 200 gm.	Steamed rice, 100 gm.
Cream, 100 c.c.	2 tablespoons butter.	Cream, 100 c.c.
Bread, 30 gm.	Spinach, liberal portion.	Milk, 200 c.c.
	Cocoa, 200 c.c.	
Calories, 2278. Protein, 40 gm. Ash alk., 59 n. Iron, 15 mg.		
III*b*.		
Cream of wheat, 150 gm.	Cream of spinach soup, 200 c.c.	Cornstarch blanc mange, 100 gm.
Cream, 2 tbsp.	Baked potato, 200 gm.	Cream, 2 tbsp.
Sugar, 1 tsp.	Butter, 2 tbsp.	Bread, butter, 30 gm.
½ orange.	Asparagus, 1 portion.	Stewed prunes.
Toast, 30 gm.	Lettuce with oil and lemon.	Cocoa, 200 c.c.
Butter.		
Milk, 200 c.c.	Graham bread, butter, 30 gm.	
	Cocoa, 200 c.c.	
Calories, 2080. Protein, 43 gm. Ash alk. Iron, 15 mg. plus.		
III*c*.		
½ Orange.	Cream soup, 200 c.c.	Ripe banana, 400 gm.
Oatmeal, 150 gm.	Potato, baked, 200 c.c.	Milk, 240 c.c.
Toast, butter, 30 gm.	Butter, 2 tbsp.	*Or*,
Cream, 50 c.c.	Spinach, 1 portion.	Cornstarch, blanc-mange, 200 gm.
Milk, 100 c.c.	Lettuce with oil, 1 portion.	Cream, 50 c.c.
	Milk, 200 c.c.	Bread and butter, 33 gm.
Between meals 2 cups cocoa and 2 slices toast.		Cocoa, 200 c.c.
Calories, 2348. Protein, 53 gm.		

There has been a tremendous amount of interest in the dietetic treatment of nephritis in the last five years. This has resulted in the introduction of new methods of analyzing the patient's blood and the food he takes, so that we can now give a diet and at the same time accurately observe its effect. The therapy of nephritis has been fundamentally altered by these investigations.

Parenchymatous Nephritis.—This is not looked upon as nephritis today. It is called a nephrosis, and is simply a functional condition in which there is inability of the kidney to excrete two substances, water and salt, In nephrosis there is little inability to secrete the nitrogen, therefore little retention of uric acid, creatinin, or urea; and from the dietetic standpoint the treatment is perfectly simple: we merely restrict the intake of water and salt. A balance is obtained by measuring the daily intake and output of salt and water. Enough water must be retained in order to maintain the salt ratio in the body fluids at $\frac{7}{10}$ of 1 per cent. Enough water must be taken in order to dilute the salt to this ratio. For example, 3000 c.c. of fluid would have to be retained in order to dilute 21 grams of salt to $\frac{7}{10}$ of 1 per cent. As much as 6 or 7 pounds of fluid may be retained in the deeper structures without producing visible edema. By depriving the patient of salt the surplus fluid in the tissues not necessary to maintain the proper ratio will be eliminated. The treatment of the edema of parenchymatous nephritis by salt retention is a most important advance in the therapy of this disease.

Interstitial Nephritis.—We come now to the principal subject of today. Our investigations of the past year have been confined almost entirely to the treatment of interstitial nephritis. Here there is practically no retention of salt and water. These patients do not have edema, but there is an enormous retention of nitrogen resulting from protein metabolism. Chart II[1] shows the extent of this nitrogen retention. The normal amount of uric acid is 2 to 3 mg., urea nitrogen is 12 to 15 mg., and crea-

[1] From "The Value of Recent Laboratory Tests in the Diagnosis and Treatment of Nephritis," Chace and Myers, Jour. Amer. Med. Assoc., September 23, 1916, pp. 929–932.

CHART II

Uric Acid, Urea Nitrogen, and Creatinin of Blood in Interstitial Nephritis[1]

Date, 1915–1916	Case.	Age.	Sex.	Diagnosis.	Condition.	Mg. per 100 C.c. of Blood.			Phthalein 2 Hours, Per Cent.	Systolic Blood-pressure.	Urine.	
						Uric Acid.	Urea N.	Creatinin.			Albumin.	Casts.
I												
9/17	H. L.	23	♂	Pulmonary tuberculosis	Unchanged.	6.5	16	2.7	58	130	++	+
8/10	E. H.	41	♂	Pericarditis	Unchanged.	5.6	13	2.1	45	150	−	−
10/12	F. D.	45	♂	Interstitial nephritis	Unchanged.	5.5	12	2.5	37	185	−	++
3/ 6	B. D.	35	♀	Diffuse nephritis	Unchanged.	9.6	19	2.4	45	175	+	++
II												
8/11	J. J.	65	♂	Early interstitial nephritis	Unchanged.	9.5	25	2.5	13	185	+	+
7/21	D. S.	56	♂	Early interstitial nephritis	Unchanged.	6.6	24	3.3	26	185	−	++
9/21	D. D.	52	♂	Early interstitial nephritis	Unchanged.	8.7	20	3.6	20	100	+	++
8/ 3	C. M.	54	♂	Early interstitial nephritis	Unchanged.	6.3	31	2.0	23	150	−	−
III												
1/ 6	L. P.	57	♂	Moderately severe chronic interstitial nephritis.	Improved.	8.0	80	4.8	0	240	++	++
3/ 1						4.9	17	2.9	10	170		
4/23	J. P.	34	♂	Moderately severe chronic diffuse nephritis.	Improved.	8.3	72	3.2	25	238	+++	++
5/21						5.3	21	1.9	43	145		
1/15	W. C.	49	♂	Moderately severe chronic diffuse nephritis.	Improved.	9.5	44	3.5	38	210	++	++
1/28						2.5	19	1.9	52	120		
IV												
4/11	E. C.	50	♀	Typical fatal case of chronic interstitial nephritis	Died.	22.4	236	16.7	0	210	++	Pus.
3/23	T. D.	34	♂	Typical fatal case of chronic interstitial nephritis	Died.	15.0	240	20.5	2–3	225	++	+
1/25	S. H.	37	♂	Typical fatal case of chronic interstitial nephritis	Died.	14.3	263	22.2	0	220	++	+
4/15	J. W.	34	♂	Typical fatal case of chronic interstitial nephritis	Died.	8.7	144	11.0	Trace.	225	+	+

[1] Normal findings: uric acid from 2 to 3 mg.; urea nitrogen, from 12 to 15 mg.; creatinin, from 1 to 2.5 mg. per 100 c.c.
The symbol ♂ signifies male; ♀ signifies female.

tinin from 1 to 2.5 mg. per each 100 c.c. of blood. In interstitial nephritis the kidney at first becomes unable to excrete the uric acid, which is to be expected, because, being eliminated with greatest difficulty, it is the substance which would be the very first to be retained. In our studies of uric acid, urea, and creatinin we find the retention of uric acid is anywhere from 6 to 8 mg., in certain cases, even where there is no retention of urea or creatinin. If the nephritis is a little more severe, the kidney also becomes unable to eliminate the urea. In most severe cases of nephritis you not only find retention of uric acid and urea, but also, markedly, of creatinin. Victor C. Myers, a professor in this institution, was the first to call our attention to the importance of the prognostic value of the retention of blood creatinin in nephritis. (Chart III.[1]) This substance on a meat-free diet is practically endogenous in origin and its formation very constant. It excretion has nothing to do with the food intake, and therefore forms a fairly good index as to the severity of the disease.

We found that in all our advanced cases the retention was from 33.3 mg. to just below 4.9 mg. per 100 c.c. With perhaps only one exception, in all cases above 5 mg. of creatinin to 100 c.c. of blood there was a fatal outcome. This substance is one of the easiest to detect in the blood, and, therefore, testing for it is practical for the general practitioner. Such a test can be made in twenty minutes. It is superior to the phenolsulphonephthalein test (which indicates only the patient's condition at the moment the test is taken) in that it shows the permanent changes in the patient's condition. This condition is apt to change from day to day.

Another factor of diagnostic value in early nephritis is the retention of a small amount of uric acid in the blood, the detection of which is confirmatory when this disease is suspected. (Chart IV.[2])

Given the phthalein output and the blood-pressure, the

[1] From "The Value of Recent Laboratory Tests in the Diagnosis and Treatment of Nephritis," Chace and Myers, Jour. Amer. Med. Assoc., September 23, 1916, pp. 929–932.

[2] Ibid.

CHART III

THE PROGNOSTIC VALUE OF THE CREATININ OF THE BLOOD IN NEPHRITIS

Case.	Blood Creatinin, Mg. to 100 C.c.	Phthalein, Two-Hour Output, Per Cent.	Termination.
1. W. F.	33.3	....	Died.
2. E. M.	28.6	0	Died.
3. S. H.	22.2	0	Died.
4. T. D.	20.5	2 to 3	Died.
5. I. D.	20.0	0	Died.
6. P. J.	20.0	0	Died.
7. E. L.	18.9	0	Died.
8. M. M.	17.8	....	Died.
9. E. C.	16.7	0	Died.
10. W. O'C.	16.6	Trace.	Died.
11. M. K.	14.7	....	Died.
12. K. K.	14.7	0	Died.
13. J. H.	14.3	....	Died.
14. E. P.	12.7	0 to 1	Died.
15. W. W.	12.5	0	Stationary.
16. M. O.	11.1	0	Died.
17. K.	11.1	0 to 3	Died.
18. J. W.	11.0	3 to 1	Died.
19. J. D.	10.7	0–5–4–3–6	Died.
20. C. G.	10.0	0	Died.
21. S. W.	9.1	0	Died.
22. V. A.	8.3	6–4–2	Died.
23. J. S.	7.4	....	Died.
24. W. G.	7.0	....	Died.
25. E. W.	6.7	5	Died.
26. A. F.	6.1	9	Died.
27. M. R.	5.9	3	Died.
28. J. McC.	5.6	2–7–10	Improved.
29. V. R.	5.5	....	Died.
30. M. N.	5.4	13–4	Stationary.[1]
31. E. E.	5.3	10	Died.
32. A. D.	5.2	....	Died.
33. T. K.	4.9	....	Died.
34. L. P.	4.8	0–10–31	Improved.

blood chemistry will check up pretty accurately with the other more or less standard findings.

Now we come to the question, How can we utilize the findings in the blood as a guide to treatment? This has been carefully

[1] This patient has since died with a creatinin of 12.5 at time of death.

CHART IV

The Uric Acid of the Blood in Cases of Incipient Interstitial Nephritis

Case.	Age.	Sex.	Diagnosis, Remarks.	Mg. to 100 C.c. of Blood.			Phthalein, 2 Hours Output, Per Cent.	Blood-pressure.		Urine.	
				Uric Acid.	Urea Nitrogen.	Creatinin.		Systolic.	Diastolic.	Albumin.	Casts.
1. J. J.	65	♂	Interstitial nephritis	9.5	25	2.5	13	185	90	+	+
2. E. B.	46	♀	Fibrillation	9.3	14	2.9	44	120	90	−	−
3. D. D.	52	♂	Cirrhosis of liver, interstitial nephritis, chronic alcoholism	8.7	20	3.6	20	100	87	+	+
4. B. D.	25	♀	General edema	7.7	20	2.6	45	168	100	+	−
5. M. K.	49	♂	Carcinoma of stomach	7.5	16	2.2	50	150	90	−	+
6. D. S.	56	♂	Interstitial nephritis	7.1	16	2.0	26	185	110	−	+
7. A. R.	57	♂	Carcinoma of stomach, interstitial nephritis	6.8	20	1.8	40	140	80	−	+
8. H. L.	23	♂	Pulmonary tuberculosis, tuberculosis of kidney	6.5	16	2.7	58	130	90	+	+
9. C. M.	54	♂	Hypothyroidism, interstitial nephritis	6.3	31	2.0	45	150	90	−	−
10. M. McA.	44	♂	Syphilis, interstitial nephritis	6.3	17	2.7	38	185	80	+	+
11. W. B.	71	♂	Chronic arthritis, arteriosclerosis, interstitial nephritis	6.1	12	2.4	65	145	80	+	+
12. E. H.	41	♂	Pericarditis, moderate alcoholism	5.6	13	2.1	45	150	65	−	−

worked out. Inasmuch as urea arises practically from the food ingested, we can keep track of the nitrogen retention by testing the urea in the blood from time to time. In passing, I might state that under the old milk régime for nephritics—which, perhaps, has been as generally used as any other—about 40 to 50 grams of urea were ingested daily in the form of milk, and much of this amount was retained. This will show you one objection to the exclusive milk diet formerly used.

In outlining a diet we should consider first the minimum protein requirement for the individual patient because he must for a time be on as low a protein intake as is compatible with good health. A nephritic requires about the same amount of protein as a patient lying in bed with some other disease. The body can maintain itself on from $\frac{1}{2}$ to $\frac{3}{4}$ gram of protein per kilogram of weight; which means that a patient weighing 150 pounds should have from 40 to 50 grams of protein a day. Our lowest protein diet begins at about 30 grams, and that amount, as nearly as possible, must be taken daily in order to maintain weight. It has been demonstrated experimentally that you can spare the body protein—*i. e.*, you can prevent a man from withdrawing energy from his own muscle—by giving him carbohydrates and fats. It is for this reason that the lemonade diet was first suggested. This enables him to spare body protein and to furnish energy intake in the form of carbohydrates. In very severe cases a pure lemonade diet comes first. Reference back to Chart I will show the amount the patient should have each day; it consists, practically, of 4 glassfuls which furnish adequate calories (1242) a day and at the same time 8 mg. of iron. A patient can maintain himself for three or four days just with 4 glassfuls of lemonade daily. After this time he will begin to draw upon his body proteins. As the muscles are drawn upon for energy his weakness will increase and utilization of his heart muscle will result in an accelerated pulse-rate, by which you can detect the process going on.

Previously and for some time it was the custom with patients in such a condition to simply give cereals with a small amount of milk. Now after a few days, the question arises, What is the

best form of protein to put a patient on after his first dietary restriction to lemonade?

Proteins.—In the first place, we must have a diet which is well balanced. Proteins are essential for the maintenance of strength, although not necessary for the energy supply; yet the lowered permeability of the kidney for the nitrogenous constituents of the urine forbids a high protein ration, for these substances must not accumulate in the blood, burdening the kidney unduly and, indeed, affecting the entire organism.

It has been shown that proteins vary in their nutritional value. Some foods are superior to others in furnishing proteins adequate to growth; such foods, for instance, as meat, milk, and eggs. Vegetables and grains, though furnishing proteins, will not alone support life and must be supplemented. These foods, therefore, are divided into complete and incomplete proteins. As the actual minimum daily protein requirement of man is not very high, in the early stages of the treatment of the nephritic his nitrogen intake should be as small as possible.

Amino-acids.—As I said before, the proper balance of the diet is the first consideration. The work of the Department of Physiological Chemistry at New Haven has shown that animals cannot live on certain types of amino-acids alone, and they would live but not grow on another type. You must supplement the incomplete proteins by a minimum amount of complete protein or incomplete protein not similarly deficient to produce satisfactory results. And, vice versa, the minimum amount of superior proteins must be supplemented by a sufficient amount of the inferior to balance the diet. For instance, gelatin, on which a patient alone cannot live, is very excellent as a supplemental food; in fact, knowledge of the value of such proteins as gelatin has been of great advantage in the treatment of disease in general.

Mineral Element.—Aside from the proper amount and kind of protein, the supply of the mineral elements is most important. We have tabulated on this chart (V^1) the distribution of mineral

[1] From "Dietetic Treatment of Nephritis," Chace and Rose, Jour. Amer. Med. Assoc., August 11, 1917, vol. lxix, pp. 440–444.

elements in some complete and incomplete protein foods. The chart shows the percentages of protein, calcium, phosphorus, chlorin and iron, and the foods rich in acid and alkaline ash. It has been demonstrated that death will come more quickly to a patient on a diet without mineral salts than to one in absolute starvation.

CHART V

DISTRIBUTION OF MINERAL ELEMENTS IN SOME HIGH AND LOW PROTEIN FOODS[1]

Food.	Protein, Per Cent.	Calcium, Per Cent.	Phosphorus, Per Cent.	Chlorin, Per Cent.	Iron, Per Cent.	Ash Balance in Terms of Normal Solution, C.c.	
Asparagus	1.8	0.029	0.039	0.040	0.0010	Base	0.81
Bananas	0.4	0.007	0.024	0.200	0.0006	Base	5.6
Butter	1.0	0.014	0.013	0.00X			
Carrots	1.1	0.055	0.044	0.036	0.0008	Base	10.8
Celery	1.1	0.071	0.044	0.170	0.0005	Base	7.8
Citrus fruit	0.5	0.036	0.017	0.010	0.0004	Base	7.0
Lettuce	1.2	0.036	0.039	0.050	0.0010	Base	7.4
Potatoes, white	2.2	0.011	0.061	0.030	0.0013	Base	7.7
Potatoes, sweet	1.8	0.018	0.039	0.120	0.0005	Base	6.0
Prunes, dried	2.1	0.043	0.011	0.010	0.0029	Base	25.6
Raisins, dried	2.6	0.057	0.123	0.070	0.0050	Base	23.7
Spinach	2.1	0.064	0.057	0.010	0.0032	Base	27.1
Cream (18.5 p. c.)	2.5	0.100	0.079	0.100	0.0002	Base	1.3
Milk	3.3	0.121	0.095	0.120	0.0002	Base	1.8
Barley, pearl	8.5	0.018	0.200	0.020	0.0013	Acid	10.3
Cornmeal	9.2	0.011	0.142	0.020	0.0011	Acid	3.7
Oatmeal	16.7	0.093	0.381	0.035	0.0036	Acid	10.6
Rice	8.0	0.009	0.087	0.050	0.0009	Acid	8.4
Rye flour	6.8	0.050	0.339	0.020	0.0040		
Wheat flour	11.2	0.019	0.081	0.070	0.0015	Acid	9.6

Iron.—In order to counteract the well-known tendency of nephritics to become anemic, special attention has been given to adding to the diet those articles of food very large in iron. Chart V shows the relative amount of iron in some of the common food-stuffs. The daily requirement of iron is 15 mg., but many patients when taking the commonly prescribed diets have an

[1] The data from which this table has been compiled are taken largely from Sherman, Chemistry of Food and Nutrition, New York, 1912.

intake much below this figure. Iron in organic combination is much more readily assimilable than in inorganic preparations. Simply prescribing iron compounds will not make up for any iron omission in the diet.

Acidosis.—Mineral salts are particularly valuable in furnishing alkaline ash. As you know, there is a well-known tendency in nephritis, particularly in the advanced stages, to the formation of acidosis with the symptom of dyspnea. This is due to the impaired elimination of the normally formed acid substances, probably acid phosphates. A certain percentage of fatalities in nephritis is due to acidosis.

Alkaline Ash Balance.—The alkaline ash balance in various foods is given in the last column of Chart V. The articles of diet which have a pronounced alkaline ash are fruits, leaves, and tubers. The ash of the grains and seeds is markedly acid.

This ash balance is a matter of a good deal of importance, not only in the treatment of nephritis, but in the ordinary diet of children to support normal growth, and also in all conditions in which you wish to balance against acidosis; that is, to give sufficient alkaline ash to attain the proper adjustment.

The importance of considering the ash balance of food-stuffs has not been thoroughly appreciated. I have known of cases of approaching acidosis that have been put on a diet of oatmeal, rice, wheat, etc., all of which have a very large acid-forming tendency. Now it is certainly very inconsistent to give a patient infusions of sodium bicarbonate to increase the carbon dioxid combining power of the blood-plasma and at the same time allow him the intake of acid-forming substances.

Even in ordinary routine practice you will encounter patients with excessively acid urine. By modifying the diet a permanent cure can be affected without the use of alkalies. A diet sheet can be made from the list on Chart V which your patient can follow very comfortably.

There is another point to be considered. It must be remembered that there are two substances in food essential to the continuance of life—one soluble in water, the other associated with the ether-soluble fraction of the food. They are minute quanti-

ties of certain organic substances known as food accessories, or vitamins. Some of the obscure affections of the nerves in association with nephritis might well be due to a deficiency in the food accessories. In hospital diets raw milk in the past has supplied the food accessory which has prevented scurvy. The antiscorbutic element is probably thermolabile. But now that the entire milk-supply of many of our large cities is pasteurized, the danger of producing scurvy in nephritics is imminent if not guarded against. To overcome this tendency it is only necessary to add uncooked fruit to the diet.

Still another important point to consider in arranging a diet in nephritis is the psychologic aspect, particularly for the ward patient. The monotony of the day for such a patient is chiefly broken up by three things—breakfast, luncheon, and dinner. He looks forward to them with an interest that must be taken into account. It is important, from this standpoint, to have the food served warm and have it appear attractive. The diet served to the sick is a dozen times more important that that to the healthy. We will not obtain the maximum effects from our diets unless greater attention is paid to making them appetizing.

Now, coming down to the practical points of our diet. No. III on Chart I contains an outline for morning, noon, and evening meals which gives a wide choice and variety; the weights and measures of the calories, protein, ash, alkaline, and iron enable you to calculate with nicety the requirements of your patient and the variety gives you the opportunity to consult his preferences to a certain extent.

You will notice that considerable use is made of the banana. This is because it is of value in furnishing alkaline ash, is low in protein, and, being mild in flavor, can be taken in quantity for some time agreeably to the patient. In fact, patients as a rule prefer the banana diet. If used raw, they must be perfectly ripe, and in this state they furnish an antiscorbutic element. They can be used cooked with perfect success, and there are two added advantages in this in that they may be served warm and they add variety to the diet.

In passing, I wish to say that in making bread for these

patients phosphate baking powder should not be used. In nephritis there is deficient ability to eliminate phosphates through the kidneys. Bread which contains considerable salt and phosphate baking powder is very apt to produce retention. The diets as planned have a relatively high calcium content; this is to meet the daily requirement, and, in addition, it diverts the elimination of phosphorus to the intestines from the kidneys. If necessary, calcium can be supplied by adding milk to the diet.

PRESENTATION OF CASES

The case of J. B., whom I will now present, has run a very interesting course (Chart VI). He is thirty-four years of age

CHART VI[1]

FINDINGS IN INTERSTITIAL NEPHRITIS[2]

Date, 1916–17.	Creatinin, Mg. per 100 C.c. Blood.	Urea Nitrogen, Mg. per 100 C.c. Blood.	Protein Intake.	Diet.
December 22–26	7.4	61		
January 5	9.7	135		
January 9	12.5	110	49	Banana and milk.
January 12	11.1	110	49	The same alternated with
January 16–23	8.8	75	49–51	Diet 2.
January 23 to February 6	7.5	50	49–51	
February 9–20	8.4	54	49–51	
February 23–27	7.7	53	49–51	
March 2–9	6.7	50	49–51	
March 13–16	7.4	45	49–51	
March 20	10.6	46	40	Diet 4.
March 23–30	7.4	47	25–40	Diet 8–9.
April 13–17	6.4	45	52	Diet 12–13.
April 20–30	6.8	41	52	Diet 12–13.
May 8–22	6.6	31	52	Diet 12–13.
May 29–July 15	6.8	33		

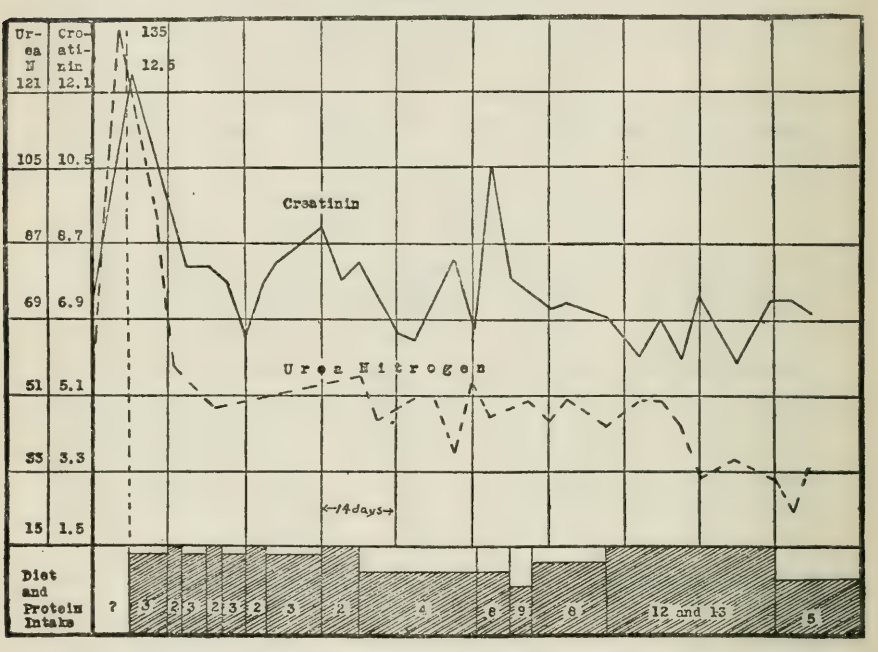
and was admitted to the Medical Ward on December 22, 1916, complaining of intense headache, orthopnea, vertigo, and mental

[1] From "Dietetic Treatment of Nephritis," Chace and Rose, Jour. Amer. Med. Assoc., August 11, 1917, pp. 440–444.

[2] J. B., man, aged thirty-four; edema, headache, dyspnea; blood-pressure, 204–130; albuminuria, hyaline and granular casts; phenolsulphonephthalein test, 3 to 19 per cent.

confusion. He was distinctly uremic. He had marked edema of the lower extremities, hands, and face. At this time his blood-pressure was 204 systolic, 130 diastolic, and his urine contained many hyaline and granular casts. Phenolsulphonephthalein test showed elimination of only 3 per cent. A glance at Chart VII will indicate the amount of urea and creatinin retained.

CHART VII[1]



Influence of the diet on the creatinin and urea in the blood in J. B., man, aged thirty-four.

This gradually increased until January 9th. The subsequent amounts of creatinin and urea of the blood have been graphically outlined in the curves on this chart; they show how the creatinin and urea in the blood have been affected by the protein intake from December 22d to May 29th.

You will agree with me that he looks perfectly well; he is now

[1] From "Dietetic Treatment of Nephritis," Chace and Rose, Jour. Amer. Med. Assoc., August 11, 1917, pp. 440–444.

able to leave the hospital and go to work. During his period under diet the red blood-cells increased from 3,300,000 to 4,200,000 and the hemoglobin from 55 to 65 per cent. He has been practically free of all symptoms for the past month. If his chemical blood-picture does not improve beyond the present, however, we must express grave doubts regarding the ultimate outcome.

CHART VIII[1]

RECENT CASES OF INTERSTITIAL NEPHRITIS

Patient.	Date, 1917.	Creatinin, Mg. in 100 C.c.	Urea Nitrogen, Mg. in 100 C.c.	Remarks.
	May 9	4.9	45	Gastric symptoms, first diagnosed as peptic ulcer.
	May 15	3.0	45	
	May 18	4.6	39	Placed on diet consisting mainly of cooked cereals, milk toast, cocoa, and occasionally banana; phenolsulphonephthalein test, 5/18, 35 per cent.
H. G.[2]	May 22	3.1	26	
Aged 21	May 25	2.6	30	
	May 29	5.7	70	
	June 1	4.7	60	
	June 8	3.3	48	
	June 15	2.5	23	
	April 24	2.8	38	Kept on diets similar to Table 4 with a protein intake not over 52 gm.; phenolsulphonephthalein test, 5/18, gave an elimination of 8.7 per cent.
	May 1	2.1	35	
J. W. C.[3]	May 8	6.1	41	
Aged 60	May 15	5.2	30	
	May 22	3.3	28	
	June 1	3.1	36	
	June 8	4.5	26	

Although the parallelism between the creatinin and urea curves in the blood and the protein intake is not as striking in this case as it has been in others, nevertheless it shows the ad-

[1] From "Dietetic Treatment of Nephritis," Chace and Rose, Jour. Amer. Med. Assoc., August 11, 1917, pp. 440–444.

[2] H. G., pain in umbilical region; no nephritic symptoms; loss of weight; anorexia; blood-pressure, 135–80; trace of albumin in urine; few casts; phenolsulphonephthalein test, 35 per cent.

[3] J. W. C., asthma; nocturnal dyspnea; edema; polyuria; blood-pressure, 190–90; small amount of albumin in urine; few casts; phenolsulphonephthalein test, 9 per cent.

vantage of being able to follow these cases accurately. In fact, it serves as a splendid check.

The next patient, H. G., aged twenty-one, shows what can be done by the dietary treatment of nephritis. When he entered the hospital on May 9th of this year his phenolsulphonephthalein test was 35 per cent. and the urine contained albumin and hyaline and granular casts. He was complaining of anorexia, loss of weight, and some abdominal pain. Placed upon Diet III in Chart I, the gradual improvement in the chemical blood findings he has experienced is shown on Chart VIII. He is now apparently well and is ready to be discharged from the hospital.

The third case to be presented, J. W. C., aged sixty, entered the hospital on April 24th of this year suffering from very marked nocturnal dyspnea, at times amounting to severe asthmatic attacks. He passed excessive amounts of urine at night and the urine contained albumin and hyaline and granular casts. Systolic blood-pressure was 190, diastolic 90. Phenolsulphonephthalein output 8.7 per cent. on admission, and since that time he has been continuously on the third diet on Chart I. He also is now free of symptoms and is able to leave the hospital and resume his work.

CLINIC OF DR. WILLIAM R. WILLIAMS

New York Hospital

TWO CASES OF EFFUSION IN THE PLEURAL, PERICARDIAL, AND PERITONEAL CAVITIES WITH ARTIFICIAL PNEUMOTHORAX

The patients shown this afternoon are two boys with many points of resemblance in their illness. The older, Case I (Admitted Feb. 23, 1915, History Number 198,724; Re-admitted May 23, 1915, History Number 200,119), was born in this country of Italian parents and is now sixteen years old. He has been employed as a hardware salesman. His family history is excellent, both parents and five brothers and sisters being alive and well. His personal history includes an attack of measles at three years of age, scarlatina at six, and a tonsillectomy at thirteen. He has had no rheumatism and no tendency to coughs. He says that his weight was 110 pounds three weeks ago and that he has lost a good deal since then.

Present Illness.—During the past two weeks he has been definitely ill, with cough with little sputum. He has had fever, headache, slight precordial pain, and a little dyspnea on exertion. He has sweated at night occasionally, vomited once, and spent most of his time in bed. On examination he did not seem very ill and had no obvious dyspnea. The mucous membranes were slightly pale, his tonsils were very large and red, notwithstanding the tonsillectomy, and his lungs showed at the left apex high-pitched breathing, exaggerated voice, and whisper. Otherwise his lung signs were quite normal. The apex-beat of his heart was indistinct. The sounds were loudest in the fifth space, 8 cm. to the left of middle line. The cardiac dulness extended 3 cm. to the right of middle line in the fourth space. To the left of

middle line it extended in the second space 3 cm., in the third space 5 cm., in the fourth space 7 cm., and in the fifth space it could not be very accurately defined, although it was obviously displaced considerably to the left. On auscultation the heart sounds were indistinct. There was a double friction-sound loudest at the base, but distinct at the apex. His pulse was 120, regular, of normal tension, and the arteries were not thickened. Examination of the abdomen was negative. Lymph-nodes were palpable in the groin, axilla, and anterior and posterior cervical regions, but none was greatly enlarged. Knee-jerks were normal. The blood contained 4,400,000 red cells, 75 per cent. hemoglobin, and 6000 white cells. The polynuclears were 60 per cent., the small lymphocytes 30 per cent., and the large mononuclears 5 per cent. Blood counts made subsequently gave practically the same figures. The urine was normal and varied from 700 to 1700 c.c. per day. His temperature fluctuated a good deal, with a daily maximum between 103.6° and 100.5° F.

The temperature was so protracted and variable that I show you the curve during his hospital residence (Chart I). On this chart we show also other data of interest in a case of serous effusion, namely, pulse and breathing rates, the daily output of urine, number of stools, and an occasional record of his weight. His pulse varied in rate from 130 to 100. His weight was 87 pounds on admission, reached 101 pounds at one time, and has fallen since then to $88\frac{1}{2}$ pounds. Von Pirquet and Moro tests were positive. His cardiac dulness increased moderately in area. The friction persisted, but he had no pain or discomfort. An x-ray of his thorax showed a very large heart area suggesting pericarditis with effusion. His pericardium was not tapped.

About a week after admission there appeared over the right side of the thorax in the back the signs of increasing pleural effusion. On March 4th right thoracentesis was performed, which yielded 800 c.c. of reddish amber liquid, specific gravity 1020, containing a large amount of albumin, and 291 cells to the cubic millimeter, all lymphocytes. The pleura seemed to have been emptied by this operation. On March 11th 500 c.c. of similar liquid was obtained on tapping the same pleura. The

effusion in the right side recurred so slowly that on the 8th of April only 25 c.c. were obtained, and practically none at a later date, although a needle was inserted three or four times because of the striking dulness that persisted there. The needle suggested the presence of a tough thickened pleural membrane.

Shortly after this signs of liquid in his left pleura made their appearance, and on March 24th a left thoracentesis was done which yielded 475 c.c. of amber liquid. This pleura behaved quite differently from the right and serum reaccumulated very rapidly. On the 6th of April 500 c.c. were removed; on the 19th, 650 c.c. The patient, feeling much better, was taken home on April 28th.

He returned, however, on May 23d, seeking readmission because his dyspnea had returned and his abdomen had begun to swell, although he had not been confined to bed. At this time the signs over his lungs were not very different from his signs on discharge from the hospital. He still had a large area of cardiac dulness, pericardial friction-sounds were heard, but the cardiac sounds were distinct. There was dulness over the back on both sides below the ninth rib, with diminished fremitus, breath sounds, and voice. Moist râles were heard throughout the lungs. His liver, which began to enlarge during his previous hospital sojourn, was palpable down to 3 cm. below the ribs in the right nipple line, and 7 cm. below the xiphoid in the middle line. His spleen was felt 4 cm. below the costal margin. There was shifting dulness in the flanks and distinct liquid wave. The abdominal veins were not distended.

His abdomen was tapped on May 24th and 2200 c.c. of clear serum withdrawn. This contained 300 cells to a cubic millimeter, and of these, 97 per cent. were mononuclears. The serous sacs were tapped so many times that it seems desirable to present the record of all the paracenteses in tabular form. In the table presented herewith you will find the dates of operations, the serous sac operated on, and the amount of liquid obtained. The character of the liquid did not change as time went one.

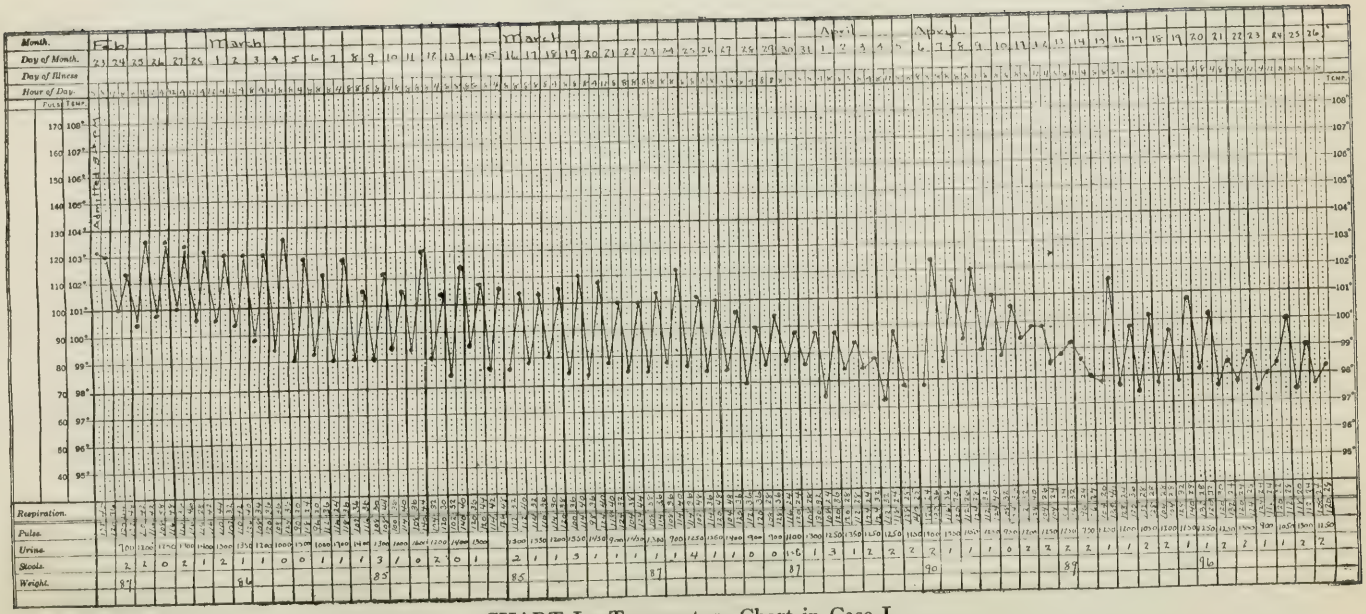


CHART I—Temperature Chart in Case I.

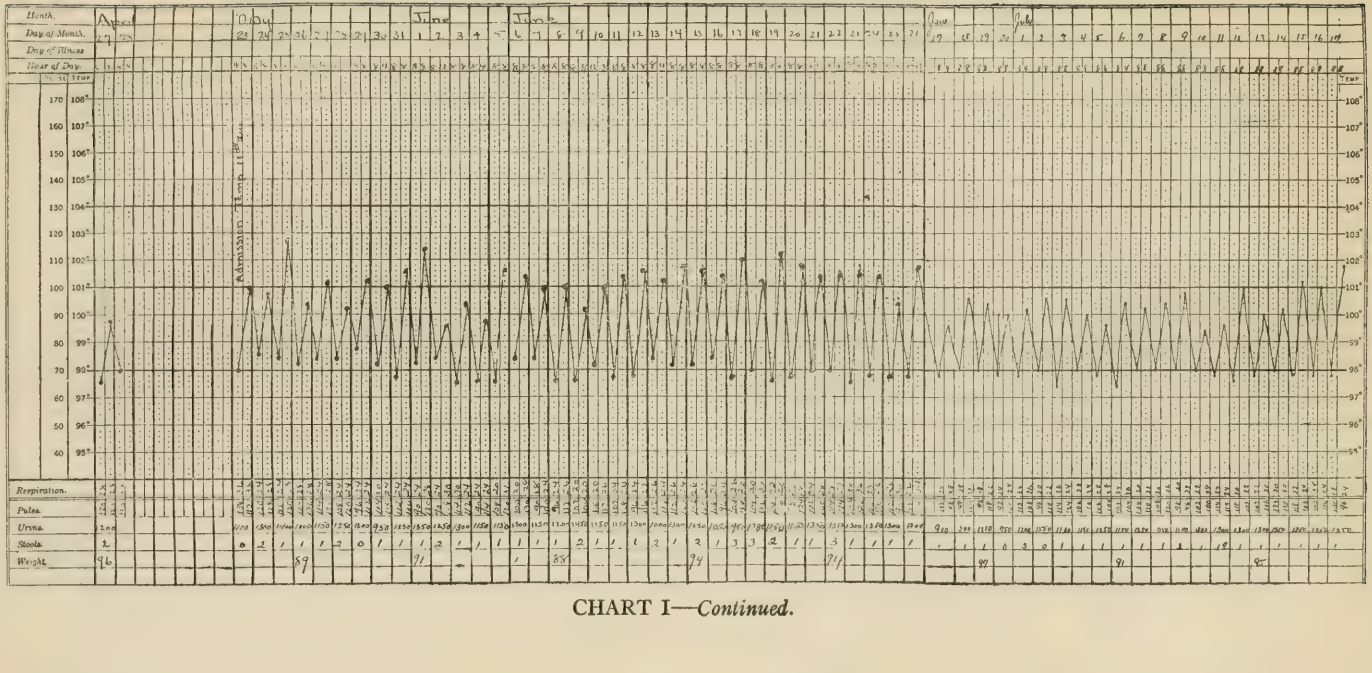


CHART I—*Continued.*

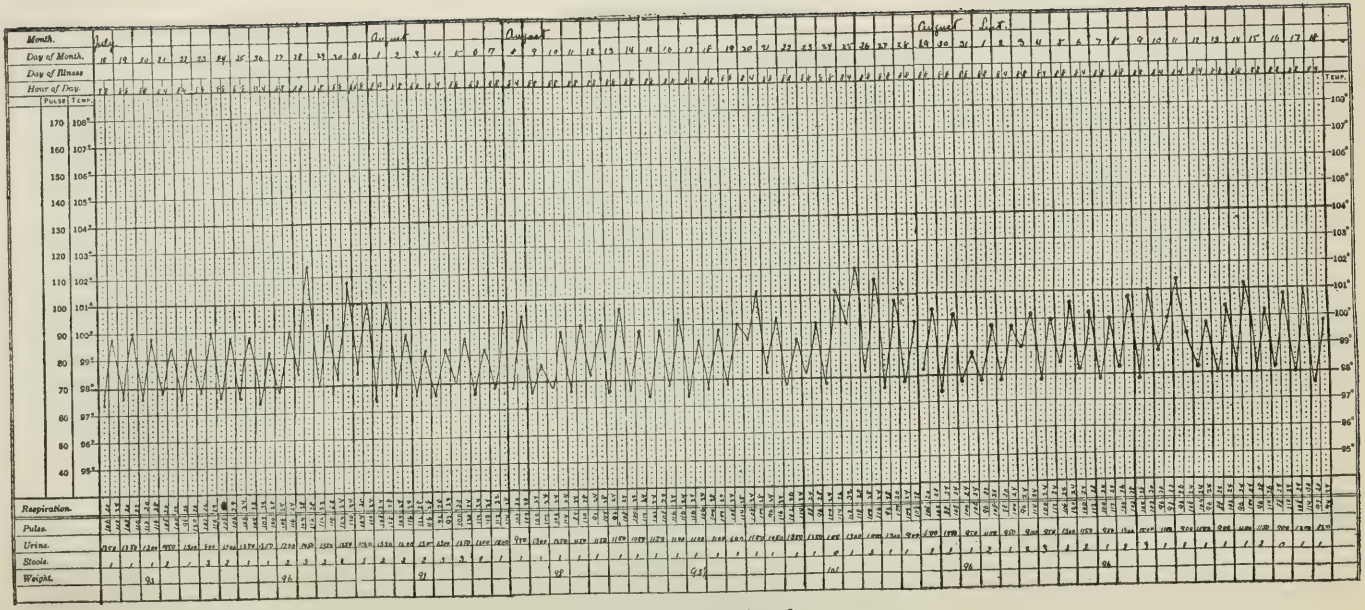


CHART I—*Continued.*

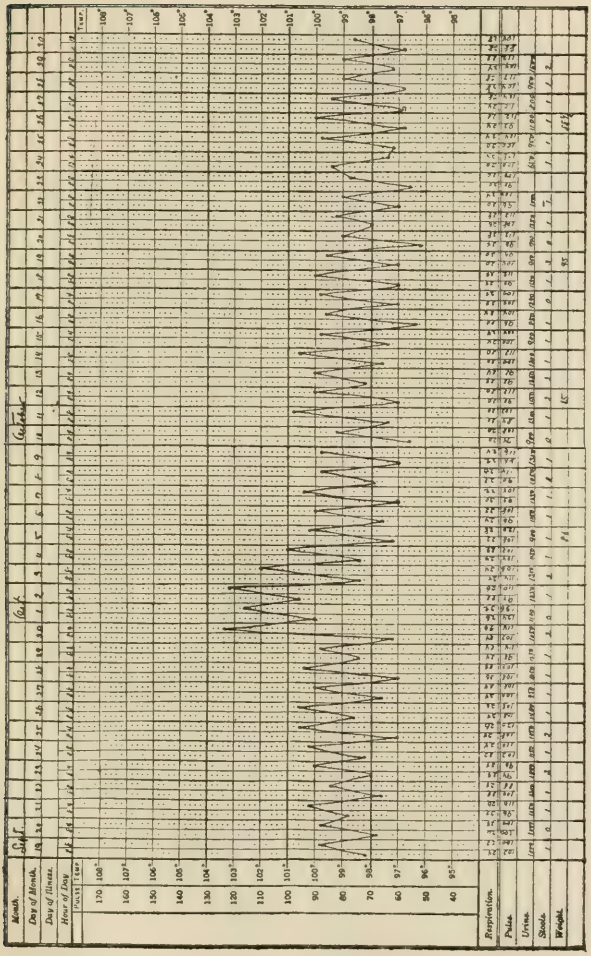


CHART I—*Continued.*

TABLE I—Record of paracentesis of Case I, giving the date of operation, the serous sac operated upon, the amount of liquid obtained, and also the amount of gas introduced into left pleura.

	Tappings			
Dates.	Liquid from right pleura.	Liquid from left pleura.	Gas introduced into left pleura.	Liquid from abdomen.
3/ 4	800 c.c.			
3/11	500 c.c.			
3/24	....	475 c.c.		
4/6	....	500 c.c.		
4/8	25 c.c.			
4/19	....	650 c.c.		
5/24	....	....	....	2200 c.c.
5/25	....	1250 c.c.		
6/5	....	1400 c.c.		
6/7	....	1100 c.c.		
6/9	....	900 c.c.		
6/13	....	1300 c.c.		
6/15	1100 c.c.			
6/17	....	....	....	1600 c.c.
6/19	....	1100 c.c.		
6/21	....	1050 c.c.		
6/24	....	550 c.c.		
6/26	....	1250 c.c.		
6/28	....	800 c.c.		
6/30	....	1100 c.c.		
7/3	....	1300 c.c.	....	2900 c.c.
7/5	....	1000 c.c.		
7/7	....	600 c.c.		
7/10	....	1000 c.c.		
7/12	....	950 c.c.		
7/14	....	1000 c.c.		
7/16	....	700 c.c.		
7/17	....	....	....	3300 c.c.
7/18	....	1100 c.c.		
7/20	....	1000 c.c.		
7/22	....	700 c.c.		
7/24	....	1100 c.c.		
7/26	....	700 c.c.		
7/27	10 c.c.			
7/28	....	1000 c.c.	1000 c.c.	
7/30	....	....	....	3550 c.c.
8/1	....	650 c.c.		
8/5	....	650 c.c.	1050 c.c.	
8/12	....	300 c.c.	500 c.c.	
8/13	....	....	....	3400 c.c.

Dates.	Liquid from right pleura.	Liquid from left pleura.	Gas introduced into left pleura.	Liquid from abdomen.
8/20	....	500 c.c.	600 c.c.	
8/24	....	400 c.c.	600 c.c.	
8/27	....	....	....	3800 c.c.
8/31	....	500 c.c.	450 c.c.	
9/9	....	250 c.c.	400 c.c.	
9/18	....	300 c.c.	400 c.c.	
9/30	....	600 c.c.	600 c.c.	
10/18	....	200 c.c.	200 c.c.	

The effusion into the left pleura was so persistent and so rapid that an attempt was made to check this by the introduction of gas into the pleural sac, that is, by the production of artificial pneumothorax. This was first done on July 28th, when 1 liter of gas was introduced. More gas was introduced whenever the chest was tapped after this time, except on one occasion, on August 1st, as is indicated in the table. The amount of gas introduced was about the same as that of the liquid removed, although sometimes the gas was admitted until the intrapleural pressure reached zero. The volume of gas introduced is indicated in the table of paracenteses. It is interesting to note that during the patient's stay in the hospital, a period of about six months, the liquid removed from the pleuræ amounted to 31,025 c.c.; the liquid removed from the abdomen was 20,750 c.c. This quantity of liquid would weigh about 115 pounds.

It is very interesting to compare the rate of accumulation of the liquid before and after the production of pneumothorax. A reference to the table will show that during July the left pleura was tapped almost regularly on alternate days, and that from 600 to 1100 c.c. had accumulated during the two days. Immediately after the pneumothorax, however, this rate of accumulation was strikingly reduced. In order to present this to your eye more sharply I have prepared a chart covering the behavior of this pleura from June 29th to August 20th. In this chart (Fig. 46) the heavy vertical lines show the actual amount of liquid removed from this pleural cavity on the day specified. The hatched area shows the average daily quantity of liquid for the various periods. The first period of the chart extended from

June 28th to July 14th. The average daily exudate during this period of sixteen days was 434 c.c. The second period was a fortnight in duration (from July 14th to July 28th) and the daily average was 450 c.c. On July 28th pneumothorax was first produced. During the next eight days the daily exudate was only 163 c.c. This fell during the following week to a daily average of 43 c.c. and has continued low since then. The interval between tappings has correspondingly lengthened, greatly to the patient's comfort.

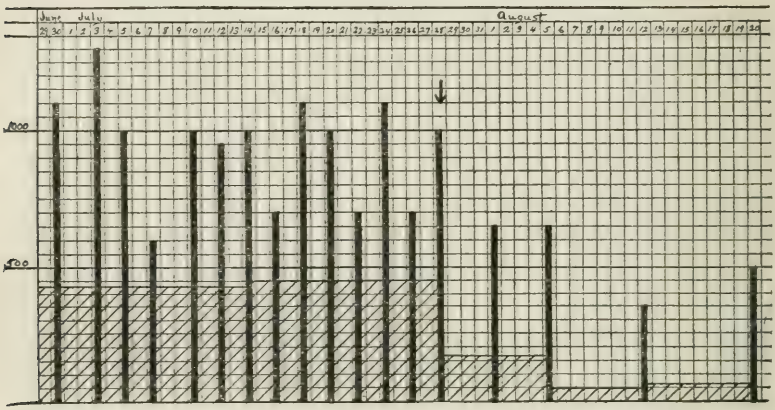


Fig. 46.—The heavy vertical lines show the cubic centimeters of liquid removed from the right pleura on the dates indicated. The arrow marks the date of the first artificial pneumothrax. The hatched areas represent the daily average exudate for the periods indicated.

The second patient, Case II (Admitted April 21, 1915, History Number 199,655; Re-admitted May 25, 1915, History Number 200,157), is also a boy of Italian parentage. He is nine years of age. His family history is good, his parents and their other children being in good health. His previous history reveals measles at two years of age and whooping-cough at five years of age.

The present illness began about two months before admission with an attack that was called grippe, which lasted three days, then improved, and then developed more severe symptoms. During the course of what was called a relapse he had scarlet

fever. Following the scarlet fever, a month ago, pericarditis was diagnosed, and two weeks ago pleurisy. The symptoms of which he complains are progressive weakness, dyspnea on exertion, and for one week abdominal distention. He has not been kept in bed.

On examination his tonsils were slightly enlarged. Over his lungs, at the apices, there was high-pitched, prolonged tubular breathing. On the right side there were many râles over the upper part of the lung and below the angle of the scapula at both bases. The area of cardiac dulness extended in the second space $2\frac{1}{2}$ cm. to the right of middle line, in the fifth space $3\frac{1}{2}$ cm. to the right. To the left of middle line, in the second space, it extended 3 cm. and in the fifth space 5 cm. The sounds at the apex were distant. The apex-beat was not seen or felt. No murmurs were heard. The liver edge was felt 10 cm. below the ribs in the nipple line, the spleen 3 cm. below the ribs. Signs of ascites were not found on admission. The reflexes were normal. His blood examinations showed 85 per cent. hemoglobin, 5,000,000 red cells, 10,000 or 11,000 white cells, with a normal differential count. The temperature was practically normal. The urine was normal.

This case resembled the first one to a remarkable degree. All his serous sacs showed effusion. Both pleural cavities and the abdominal cavity were tapped. The pericardial sac showed signs of effusion, but it was not tapped at any time.

The details of all of these tappings are presented in tabular form in Table II. The table shows the date of operation, the cavity operated upon, and the amount of liquid obtained. The liquid obtained from this patient was clear straw-colored serum, very rich in albumin, containing a moderate number of cells, of which from 94 to 95 per cent. were mononuclears.

A pneumothorax was resorted to in this patient also. You will remember that in the first patient the exudation of the liquid in one pleura decreased to practically nothing after a few tappings, so that we had only the remaining pleural cavity to deal with. In this patient also one pleura, the left, behaved very well, so that it became feasible to make use of artificial pneumothorax

TABLE II—Record of parancentesis of Case II, giving the date of operation, the serous sac operated upon, the amount of liquid obtained, and also the amount of gas introduced into the right pleura.

Dates.	Tappings			
	Liquid from left pleura.	Liquid from right pleura.	Gas introduced into right pleura.	Liquid from abdomen.
4/23	....	500 c.c.		
4/27	600 c.c.			
4/30	....	600 c.c.		
5/4	500 c.c.			
5/8	....	400 c.c.		
5/10	400 c.c.			
5/13	....	600 c.c.		
5/26	....	....	....	800 c.c.
5/29	....	850 c.c.		
6/3	400 c.c.			
6/5	....	800 c.c.		
6/7	....	800 c.c.		
6/9	....	700 c.c.		
6/11	....	600 c.c.		
6/13	300 c.c.			
6/15	....	650 c.c.		
6/17	....	600 c.c.		
6/19	....	600 c.c.		
6/20	50 c.c.			
6/21	....	650 c.c.		
6/23	....	600 c.c.		
6/25	....	600 c.c.		
6/28	....	550 c.c.		
7/3	....	800 c.c.		
7/5	....	700 c.c.		
7/7	....	650 c.c.		
7/10	....	850 c.c.		
7/12	....	700 c.c.		
7/14	....	800 c.c.		
7/16	....	650 c.c.		
7/18	....	600 c.c.		
7/20	....	650 c.c.		
7/21	....	....	....	1000 c.c.
7/22	650 c.c.			
7/24	....	700 c.c.		
7/25	350 c.c.			
7/26	....	750 c.c.	750 c.c.	
7/28	....	400 c.c.	400 c.c.	
8/1	....	700 c.c.		
8/6	....	850 c.c.	700 c.c.	

Dates.	Liquid from left pleura.	Liquid from right pleura.	Gas introduced into right pleura.	Liquid from abdomen.
8/11	....	500 c.c.	600 c.c.	
8/17	....	400 c.c.	800 c.c.	
8/23	....	500 c.c.	500 c.c.	
8/31	....	700 c.c.	700 c.c.	
9/9	....	600 c.c.	700 c.c.	
9/18	....	600 c.c.	600 c.c.	
9/23	....	....	....	1300 c.c.
9/30	....	600 c.c.	600 c.c.	
10/12	....	1100 c.c.	400 c.c.	
10/15	....	....	....	1400 c.c.

on the right side. In the table the quantities of gas injected are also shown.

It is interesting to note that in this case, in a space of about six months, the liquid removed from the pleuræ amounted to 28,150 c.c.; the liquid removed from the abdomen 4500 c.c. This total quantity of liquid would weigh about 72 pounds. We also show a chart similar to that representing the first case in which the amount of liquid withdrawn from the right pleura is represented by the solid vertical line, the hatched area representing the average daily accumulation of liquid for the interval between the tappings. It will be seen from a glance that this chart (Fig. 47) shows there was no tendency for the accumulation to abate up to July 26th, but that its level was practically constant. On this date a pneumothorax was first performed, 750 c.c. of gas being introduced. Immediately after, the accumulation of liquid showed a striking decrease, and this low rate persisted throughout. This chart covers a period of a few weeks before and after the beginning of pneumothorax.

The inflammations affecting all the serous sacs have been called by many names as attempts have been made to pick out sundry etiologic and pathologic groups. Some of these terms are polyorrhymenitis, polyserositis, multiple hyaloserositis, Pick's pericarditic pseudoscirrhosis of the liver, and Concato's disease. The conditions included in these terms are chronic. They show a thickening of some or all of the serous membranes and of the capsules of the contained organs, especially those of the spleen and liver. Many infectious diseases have been invoked as causes and some writers have attempted to exclude this or that specific cause.

It seems to me, however, that our knowledge at present is so confused that it does not seem helpful to be too insistent upon the use of any of these terms. In the cases presented to you today we have demonstrated the strong presumption of the existence of tuberculosis. In one of the cases tubercle bacilli were demonstrated in the liquid from the pleura. In both the Von Pirquet test and Moro test were positive. The *x*-ray photographs were reported by the radiographer to show tuberculosis, and signs in the lung bear this out. These data I think justify the diagnosis of a tuberculosis in both of these patients, and I therefore

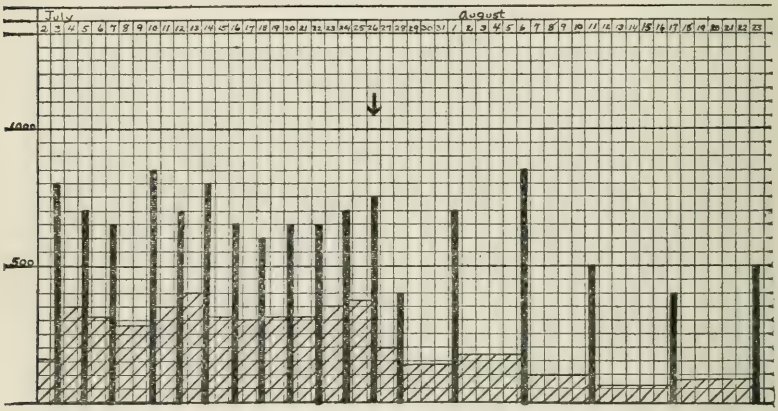


Fig. 47.—The heavy vertical lines show the cubic centimeters of liquid removed from the right pleura on the dates indicated. The arrow marks the date of the first artificial pneumothorax. The hatched areas represent the daily average exudate for the periods indicated.

present them to you as cases of extensive tuberculous lesion, illustrating in an interesting manner a helpful therapeutic maneuver.

NOTE.—The history of these patients after discharge from the hospital is not fully known. The first case, however, went to Bellevue Hospital, was transferred to some institution in the country, and was lost track of in May, 1916, about six months after he left the hospital. The second patient was transferred to a sanatorium and died about five months after he was discharged from the New York Hospital.

CLINIC OF DR. HOMER F. SWIFT

PRESBYTERIAN HOSPITAL

RHEUMATIC FEVER

Etiology—An Entity as Definite as Any of the Infectious Diseases.

Bacteriology—Organisms Found to be Members of a Large Group of Non-hemolytic Streptococci.

Treatment—The Salicylates; How They Are Absorbed; Their Distribution in the Body. Do They Increase Acidosis? Their Effect upon the Gastro-intestinal Tract; Metabolism; Circulation; the Kidneys; Antibody Production; Temperature; Auditory Organs, etc. The Natural and Synthetic Salicylates; What They Do in Clinical Conditions; Idiosyncrasy for the Drug; Dosage; Specific Action of the Drug and How to Handle the Patients with Salicylic Acid.

April 17, 1917.

THERE are two subjects I wanted to cover today, one the etiology and the other the treatment of acute rheumatic fever. The first we can talk considerably about, that is, the etiology, without being very exact, but so many statements have been made that it seems to me it is worth while to try to crystallize things to find out what we don't know, and in that way to make progress toward what we do know.

From what you have seen of this malady in the past year—and particularly in the past month or two—it does seem as if we have a disease that is an entity as definite as acute lobar pneumonia or scarlet fever or measles or any of the infectious diseases. If that is true, we should expect that there would be some specific etiologic agent, and personally I believe there is. The disease has certain characters of an infectious disease; for

example, you know it occurs in epidemics in this country in the late winter and spring months, and tapers off so that there is less in the summer and very little in the fall. If we take the three diseases—typhoid fever, lobar pneumonia, and acute rheumatic fever—you will note that typhoid fever occurs in the late summer and fall. About the time it is dropping off, you begin to get your acute lobar pneumonia, and then that curve goes up and down; about the time it goes down, acute rheumatic fever occurs, Now we know two of those diseases have quite specific etiologic factors, but there is no reason to believe that the other one may not have. A study of the disease for a great many years in a great many cities has shown that there are certain usual signs; that is, one year there will be few cases relatively, the next year more, and the next year more, so that covering a period of twenty or thirty years you will get curves of increase and decrease. That is what you see in epidemic poliomyelitis, in epidemic cerebrospinal meningitis, and it is another characteristic of infectious diseases. Then again it occurs more in certain districts than in others. These districts are often where drainage is not good and where dampness exists. It occurs in certain houses; this again may be merely a contributing factor. There is a decided tendency for the disease to occur in families. Now that may be explained by the infectious agent being carried by one member of the family and distributed to others; on the other hand, it may be explained by predisposition in certain families.

The relationship of angina and sore throat I have taken up previously. Certainly as the cases come and go, we see that there is a decided frequency of sore throat preceding the attacks of acute rheumatic fever.

Now what are the views as to the direct etiologic factors of disease? There is the possibility that it may be a bacterial disease. As you know, a number of years ago some French observers described a bacterium which was much like a Gram-negative organism, but which later was proved to be a contamination. The other great group of organisms that has been discussed comprises the cocci—staphylococci and streptococci. In the early days of bacteriology both these organisms were

described; for example, about twenty-five years ago Singer, in Vienna, found both staphylococci and streptococci in the blood-cultures and particularly in the urine of cases of acute rheumatic fever. Now you know that the finding of organisms in the urine, especially those of the coccus group, is another thing we have to accept with a great deal of reservation. Wassermann and some co-workers of his found in a case of chorea with joint symptoms a streptococcus which had a relatively low virulence and one with which they could produce in rabbits arthritis of the non-suppurative type. Following that a man named Meyer, in Berlin, and about the same time Poynton and Payne, in England —and you will hear the name Poynton and Payne quite frequently in connection with these studies—brought forward their idea of a specific streptococcus. They obtained from the blood-cultures, from the throats, and from the heart valves of a number of cases a streptococcus which when injected into rabbits produced arthritis of the non-suppurative type which cleared up after a time. These rabbits at times had pericarditis, at other times endocarditis, and for these reasons they thought that their organism was a specific streptococcus or micrococcus and diplococcus rheumaticus, so they applied the adjective "rheumaticus" to it. About the same time a man named Menzer, in Berlin, working in another clinic, found that he could get streptococci from the throats of non-rheumatic people that would produce arthritis of a similar character as in rabbits, and for this reason he claimed that you had no right to call the organism specific "rheumaticus," but explained that while the disease is a specific disease, it is due to a later reaction on the part of the individual and is not due to any peculiarity in the type of streptococcus. I might mention here in passing that in the past two years Dr. King in this city, a throat specialist, has, with the aid of Dr. Connellan, isolated from the throats of a number of rheumatic fever patients a Gram-negative chromogen—that is, a Gram-negative coccus that produced pigment—and he claims that this is a specific etiologic factor in rheumatic fever. Now had these investigators gone back to the work of other bacteriologists in this city they would have learned that a whole group of

Gram-negative chromogens had been found in the throats of many people which have not, as far as we can determine, any specific character at all.

Now the other view in reference to the streptococcus is that of Rosenow, about which you have probably read a good deal. Rosenow claims to have obtained from the joints, from the blood, and from the throats of patients with acute rheumatic fever a streptococcus, ring producing, which when injected into rabbits produced similar symptoms, and Rosenow has brought forward the idea of the organisms being endowed with the property of elective affinity, that is, as if the organisms had the property of going straight to the diseased tissue in the patient or in the animal, as the case may be. Now this property of elective affinity unfortunately is not a permanent property of organisms. They lose it and gain it; therefore, Rosenow's findings do not offer much of practical use, because if in a generation or two the organisms lose their specific affinity, you can readily see how amenable such organisms are to experimental methods.

From the standpoint of the patient, on the other hand, a certain amount of work has been done to show that the joints may become hypersensitive, that is, the tissues may become hypersensitive. Dr. Faber at the Rockefeller Hospital two years ago injected into the joints of rabbits a streptococcus, or rather killed streptococci; thus he sensitized the joints. If later he would inject into those rabbits intravenously similar organisms, the rabbits would always have an arthritis of the joints which had previously been sensitized. That seems to be a fact. How it explains the peculiar symptom complex we get in rheumatic fever is more than I can say. In these rabbits there was no cycle of involvement of joints such as we see in human beings. It may be that our picture is one of hypersensitiveness. You will recall that man who had polyarthritis in which there was more or less cyclic involvement of the joints. It is conceivable that a similar sensitiveness may occur in a bacterial disease. That is merely an hypothesis which we can bring forth; the proof of it remains to be established.

Now what do we know about the streptococcus that is iso-

lated from acute rheumatic fever? This is a subject upon which Dr. Consella and I have been working for three years, and I thought it might be of interest to you to review that work, only very briefly. We have made blood-cultures in a large series of cases. In 8 per cent. of these cases we have obtained a streptococcus from the blood-culture, once in each case, excepting one that I shall mention later. These streptococci have been studied from the cultural point of view and from the immunologic point of view. Immunologically they were studied by means of complement-fixation reactions, and rabbits were immunized by each one of the individual organisms and the reactions of those organisms to the other kind of the immunologic group were studied. Only in that way could we group these organisms at all. And this chart here shows the result of such a study. Now these organisms—28 in number—were obtained from cases of rheumatic fever, and from the disease known as subacute bacterial endocarditis, described by Dr. Libman—a different disease from acute rheumatic fever, and the source of which was the throats of patients with acute tonsillitis. I bring this chart before you just to show you that the organisms as we obtained them fell into a single group, that is, the organisms 1, 2, 8, 10, 15, 16, 19, 21, 22, 23, 26, and 27 were the ones that we obtained from acute rheumatic fever. I don't know whether or not this thing is entirely clear to you. To go into the whole subject of immunologic studies would take a whole hour, and the results would not benefit you a great deal anyway, so we shall summarize our study briefly thus: These rabbits, 28 in number, were each injected with a different organism, and then the serum from the first rabbit, let us say, was tested against all 28 of these organisms; and you will see, for example, that the serum of rabbit 1 reacted only with its own antigen, the serum of rabbit 2 reacted with others, the serum of rabbits 3 to 7 reacted with a number more. The other point in this chart I want to bring out is the general grouping of streptococci from the immunologic point of view, and that is a more general method of grouping than agglutination or protection, as in them these organisms do not fall together at all. With such a chart as this, this arrange-

ment is followed so that two organisms are away on the other side from the others. All we can say about the organisms from this point of view is that there is no such organism as Streptococcus rheumaticus, if these were specific organisms; that they are merely a part of the general group of organisms of non-hemolytic streptococci. That is the point I want to bring before you. I don't know of any more recent study than this, and I think we have to leave it at that place.

Now there is still one other point that should be brought to your attention, and that is that these organisms, when we tried them with the serum of the patients from which we obtained the organisms, the serum of the patients did not show antibodies to them. On the other hand, the serum of the patients with subacute bacterial endocarditis did show antibodies, so that in this way we feel pretty sure that with the organism as examined today in this disease antibodies were produced. In this disease, rheumatic fever, we don't know whether the organisms have anything to do with the disease itself in the production of antibodies. Is that point clear to you? So that we cannot say that these organisms are anything more than accompanying organisms. I think that without doubt in a number of cases of rheumatic fever we do get non-hemolytic streptococci, but it is yet to be proved that in every case we do get non-hemolytic streptococci. In fact, out of 6 patients with acute rheumatic fever which I have had, only half of them showed streptococci from the valves. Now you would think that that would be the one place you would get organisms constantly if they were etiologic factors, but this has not been true in our experience. You may recall that little girl with subcutaneous nodules. We obtained four different types of non-hemolytic streptococci from her heart valves. Those were classified by means of fermentation reactions. So that you can readily see that there is a great deal more work to be done in the etiology of the disease. Now I think we often gain more by acknowledging our ignorance than by presuming that we really do know something. I don't wish to say that these organisms have nothing to do with acute rheumatic fever; I do wish, however, to leave the impression that

it has not yet been proved that they have anything to do with it. As far as we can say, the organisms we have found were members of a large group of non-hemolytic streptococci.

The other subject I want to take up is the subject of salicylates. Now in your pharmacologies and in your therapeutics you will not be able to find a great deal about salicylates. A good deal of work is being done, and I shall tell you of some of these results relating to the subject in which I am interested at this time. I want you again to feel that these are subjects for thought and not for dogma. Let us first study the properties of the salicylates. They have certain antiseptic properties, *e. g.*, they inhibit putrefaction. You may recall that the question of salicylates was brought up recently in the preservation of meats, fruits, etc. They do inhibit putrefaction. They kill anthrax bacilli in a dilution of 1 : 1500, and inhibit staphylococci in a dilution of 1 : 655. Other organisms are inhibited in about the same proportion, from 1 : 500 to 1 : 2000. That is, the salicylates, as well as salicylic acid itself, possess a large amount of antiseptic property.

How are the salicylates absorbed? If you want to have salicylates absorbed from the skin, what vehicle would you use? You would use an oil or a grease. Salicylates are absorbed from the skin either through fat or alcohol as vehicles. Salicylates are practically all absorbed from the stomach and from the intestinal tract, and very little salicylate is excreted in the feces.

Salicylates are found in practically all the body tissues and fluids. Lately Hanzlik and Scott, who are studying the pharmacology of salicylates in Cleveland (their work represents the most recent work), have found that the distribution in the blood and in the joint fluids is practically the same, that is, the concentration is the same. Perhaps the percentage of concentration in the joint fluids is a little less than in the blood. An interesting fact these authors have brought forward is that in the blood of acute rheumatic fever patients, during the febrile period, concentration is less than in any rheumatic patients. One point they have not elucidated is that perhaps the febrile state causes the destruction

of salicylates. If they would compare rheumatic fever patients with other patients in which a similar febrile condition is present, would it still be proved that there is less salicylate in the blood of rheumatic fever patients? They have not controlled the work to see whether there is a similar diminution in the blood of pneumonia, we will say, or scarlet fever patients. This on the face of it is a suggestive point. It may be merely a febrile decrease. The form in which salicylate exists in the body fluid—sodium salicylate—is so much less antiseptic than salicylic acid, and is found in such weak concentrations compared to the antiseptic actions, that there has been considerable discussion as to the form in which it does exist in the body fluids. Hanzlik and Scott, however, think it must exist in the form of a sodium or some other salt of salicylic acid, and not as salicylic acid itself, because by employing the ferric chlorid test to detect free salicylic acid they have found practically none in the joint fluids, and this is the place you can study it most readily.

It has been claimed—and you will see this point in very recent books—that the administration of salicylates increases acidosis; that by pushing the drug you get symptoms of acidosis. Hanzlik and Scott studied that point and found no change in the hydrogen-ion concentration or diminution in buffer salts in patients who were given salicylates pushed to the toxic limit. Hence the fear which has been brought forward that CO_2 in the joints—the condition of acidosis, in other words—might cause the sodium salicylate to be changed into salicylic acid, and it seems to me this is as far as we can go, and that that theory will have to be done away with.

The salicylates are practically all excreted in the urine, largely in the form of salicyluric acid, and the study of this is practically impossible, as it produces Fehling's reaction, so that it cannot be said that there is sugar in the urine of a patient who has been taking salicylic acid; and this is often a source of trouble, because only yesterday we wished to make the sugar test in the urine of a patient who had been having salicylates. Another point brought out is that salicylates are excreted for about sixty to seventy-two to seventy-five hours after their

administration has been stopped. Someone asks why not get rid of it before making the sugar test. You can, of course, in this way get the sugar test and make a differential point.

Now as to the effect upon the gastro-intestinal tract: As you know, it is directly irritating, causing nausea, vomiting, and diarrhea, and in large doses ulceration may result. These symptoms appear more when salicylic acid is given than when sodium salicylate is given.

As to the effect upon metabolism: It is said to have increased metabolism. Whether or not that is so I believe we cannot say as yet, because metabolism studies have not been carried out in calorimeters, the only way you can determine metabolism accurately.

As to the effect upon circulation: In toxic doses you get a fall in blood-pressure, while in therapeutic doses you do not get this fall as a rule. Occasionally you get arhythmias such as I have mentioned previously as occurring in rheumatic fever, but the trouble is to determine whether arhythmias are due to the disease or to the drug, and that is always a point that comes up for discussion. You remember I showed you a case with Aschoff bodies; certainly the heart in that case was badly riddled with disease, rheumatic myocarditis; so it is difficult to say whether in therapeutic doses we have any disturbance of the heart. This is a point that has been brought up to you, I know, because you have asked me about the use of salicylates in cardiac disturbances, and evidently some of the men you have heard have said you should not use them when the myocardium is involved.

As to the effect upon the kidneys: When the drug is given to the point of toxicity there is practically always diminution in urine output. Now the weighing of patients has shown that many of them increase in weight at this time; so that it is thought that there may be some invisible edema. The study of renal functions has shown in some patients a diminution in phthalein at this time; in others no disturbance; in some increase in nitrogen, in others decrease, and in others no disturbance at all. In other words, there is no constant disturbance of kidney function except water output, and that is constantly disturbed at

the time of toxicity. In rabbits, dogs, and cats which have died at the point of toxicity or which have been killed, there is practically always cloudy swelling, and another point that I should mention here is that the urine at this time always shows an increase in albumin if albumin has previously been present; or if not, an albuminuria begins to appear. At the same time you get blood-cells and peculiar bodies which, to the inexperienced observer, look like casts, but seem to be a conglomeration of leukocytes in true cases. If casts appear at all, they come a little later.

As to the effect upon antibody production: As far as I have been able to determine there is only one work in which antibody studies have been made, and that was on the effect on antibody production: in this the writer states that no effect was observed. Lately I have been studying this point, but the work has not been published; it is in the process of completion. I have not found that it had any effect upon the production of agglutinins, either increase or decrease. Control animals and animals receiving salicylates all show the same general type of antibodies, both as to time of appearance and as to quantity of antibodies.

As to the effect upon temperature: It is antipyretic. In experimental fever there are certain statements that it diminishes fever in infected rabbits. However, in following the temperature curves in these rabbits I have not been able to see any effect upon the fever of rabbits that were injected with the streptococci or pneumococci. It does increase diaphoresis and causes sweating. When you get patients toward the toxic dose, they sweat, more particularly with aspirin. All who have taken aspirin know that.

As to the effect upon the auditory organs: In animals injected or poisoned with it, there is injury to ganglion cells and auditory tracts, so that the ringing in the ears that we get is explained on a real etiologic basis.

Now what are the salicylates that we ordinarily use? I think they are for most of us two, but for most of the people in the country four—sodium salicylate, methyl salicylate (oil of wintergreen), aspirin, which is salicylic acid, and diplosal.

As regards the toxic dose, a point that you will hear and read about is that natural salicylates, salicylates made from oils, are less toxic than synthetic salicylates. In a true study carefully worked out at the American Medical Association it has been proved that synthetic salicylates are no more toxic than natural ones. The mean toxic dose of sodium salicylate for males is 180 grains, for females 140 grains; of methyl salicylate, for males 120 minims, about the same for females; of aspirin, for males 165 grains, for females 120 grains; with diplosal the toxic dose is less and early seen because it is double salicyl salt, for males 100 grains, for females 80 grains. One point that is brought up in connection with this is that the administration of sodium bicarbonate with a proportionate amount of salicylic acid decreases the toxicity. Scott and Hanzlik tell us this is not so. By studying the point of toxicity in patients receiving bicarbonate and sodium salicylate or sodium salicylate alone, they found it was practically the same. However, the administration of sodium bicarbonate with sodium salicylate does seem to be less irritating to the gastro-intestinal tract.

Now again in clinical conditions; what do the salicylates do? They act as antipyretics; they act as anodynes, that is, they decrease pain; and as antiseptics. These are the three actions. Synchronous with the fall in temperature and with the clearing up of pain, there is diminution in the local joint signs and symptoms. The salicylates do not decrease the complications of the disease. I think this statement has to be modified a little, because probably fewer patients die as the result of treatment with salicylates, and certainly the period of convalescence is shortened. They don't come out of the disease wrecks as they formerly did. They come out of the disease in fairly good condition except for their heart lesions which might have arisen as a result of the disease. Complications of the disease occur in practically the same way. Another thing that has been brought forward by Dr. Joseph Miller of Chicago is that in a study of cases treated and untreated, he found that the course of the disease in untreated patients was practically the same as in those treated. However, the difference in the comfort of the

patients, loss of weight, anemia, etc., in the two groups was striking.

Now it may be worth while just to show you two or three patients that you have seen before, and I think that means more than to tell you too much. These patients that I am bringing in have all been down before. This man was in last week, and he illustrates one point. He came into the hospital with stiffness of a number of joints and inflammatory symptoms, redness, pain, and swelling. He was started on 80 grains, and those who are near enough can see by this chart that there was continual outbreak in new joints until we had increased the drug to 160 grains. There was a febrile condition until that time. When we got up toward 160 grains, the fever came down and with it there was diminution of the symptoms in the joints that were first involved. After the patient had been on 160 grains for four days the joints all cleared up, except for a little stiffness. It is necessary to push the drug well toward the toxic point in many patients. I think with this patient it might have been better to have started with 120 grains. That is the usual dose, 120 grains a day, but it was necessary to raise it still more with this patient. Another thing we have done with this patient is that after getting it up to that point, instead of stopping abruptly, the drug has been tapered off. This man has some signs of cardiac involvement. Today there is a little increase in temperature, but he has had a stomach upset. We cannot find any new symptoms to explain it. You may recall that I mentioned to you that when you see shifts in temperature you should look for visceral complications. It is possible these are due to the drug. He is getting now 60 grains of salicylate a day. That is one type. About 60 to 75 per cent. can be recovered in the urine; the rest is destroyed. With febrile conditions there is more destroyed.

Another thing: there is an idiosyncrasy for the drug. That is what I wanted to mention in this patient. This patient has had some symptoms of joint trouble for two months, and she also has cardiac involvement, mitral insufficiency, and we think perhaps some myocardial degeneration. She came to the dispensary once or twice and was given sodium salicylate, but the

joints did not clear up. She came into the hospital with knees and ankles involved and slight involvement of the hands. She was given 120 grains of salicylate for two days and then more joints became involved. At the end of five days we had to stop because she was showing gastro-intestinal symptoms and had some ringing in the ears; 120 grains approach the toxic dose for a woman of her weight. We were not helping the joints a great deal, so we switched from one form to another. I don't know why it is, but it is a clinical fact that when we switched from sodium salicylate to aspirin there was a rapid clearing up and the patient had no more toxic symptoms. On Sunday she began to have some little nausea and ringing in the ears on aspirin, and all treatment was stopped. This morning after having free joints for two or three days, both the knee and ankle are again involved. So that about the time from Sunday morning until today is not quite the maximum period in which salicylates would be excreted, but it is getting along toward the time where there is very little salicylate to act. About that time there is recurrence of joint symptoms; this is an important point to bear in mind. There is a thing we all have to learn by experience, that it does not do to withdraw salicylates too rapidly. It might have been better in this patient not to have withdrawn salicylates in the form of aspirin altogether, but to have reduced the dose by half.

I shall just show you the charts of these patients because they are type cases, and I think you have seen examples of various types (we have tried to show them with the lantern). I shall not go into the history of these patients, but they are cases which illustrate the action of the drug. I don't think that we care so much about seeing the exact joints. What we would rather see is as much of the joint chart as we can, the temperature which is here, and the drug. This patient had only involvement in the hands and arms and was given 100 grains of salicylate a day. The temperature, you will see, rapidly fell to normal. At this time we had to stop it for a day because of toxic symptoms, but the joints cleared up entirely, and from that point on aspirin was given instead of sodium salicylate, and the temperature

stayed practically normal. At this point the febrile rise was due to tonsillectomy which was done at the time. That is a mild case which shows rapid response.

Now the next case. Here's a patient who had fairly high fever with pretty general polyarthritis, in which there was rapid decrease in the temperature with a synchronous decrease in joint symptoms. At this point the patient felt so much better that he decided to go home, and he did go home. It is a question whether we do well with every patient to help the pain. Pain may be a conservative process; it certainly is in rheumatic fever where it is necessary to give the heart a prolonged period of rest, and this is a thing you will find requires all the skill of the physician—to keep a patient who is free from pain in bed and quiet, which is so necessary for him. These two cases cleared up very rapidly.

In this case we obtained the history before the patient came into the hospital. There was ankle and feet involvement several days before admission. Temperature was 103° F. on admission and there was more involvement for a day or so until the patient got under the effect of the drug, which was 150 grains in this case. Then the joints cleared up very quickly. You will see that while in those other patients there was a clearing up of the joints immediately, in a patient of this type there was some little involvement of these joints for ten days after the others cleared up, but again the drug was dropped and the patient went on without any further complications. That is a little more severe type of case.

Now for the next case. Here is a patient from whom we got the history for about ten days before admission; he happened to be an intelligent patient and was able to tell how the joints became involved and the therapy employed. For example, the wrist-joints were involved for four days, then the elbows, and then the metacarpophalangeal joints; then the ankle became involved. This is the point where the patient was admitted to the hospital. Here the patient again received 150 grains. This day there were some toxic symptoms and the drug was decreased, but not stopped. The temperature kept up and at this point there were

again toxic symptoms, nausea, and vomiting, so the drug was changed to the form of aspirin. On a smaller dose of aspirin the temperature came down and at the same time all joint symptoms cleared up. The switching to another form of the drug was certainly beneficial in that patient, and the symptoms cleared up and remained so. You will notice that in all the patients whom we can make stay in the hospital we don't stop the drug for more than a day (if we do stop it), but switch to the other form and taper off.

Now this case illustrates that point again, general polyarthritis. The patient was receiving 150 grains of sodium salicylate, the temperature was going down, but toxic symptoms were appearing, and after the drug had been stopped two days the temperature began to go up again, more joints appeared involved (and it took up to this point, two days, for the joint involvements to reappear), and it was not until after three days of administration of the drug that there was any sign of diminution. Now this is a thing you see that is so discourgaing with many patients, that in spite of giving drugs to the point of toxicity, there will be some residue of tenderness and pain in the joints and often stiffness that will continue for a long time, and also the patient will continue to show some mild fever. Let us see how long it took before we cleared the joint symptoms up. It was a matter of three or four weeks before the joint symptoms in this case cleared up. The patient was watched to be sure of no recurrence and remained normal for three months. This is the type of patient in whom you so often get recurrences of joint symptoms.

This is the last chart, and I bring this before you to show you what you should not do. We made the mistake and you should profit by it. This patient had general polyarthritis. After two days of 150 grains, on the third day the patient vomited. It did not affect the temperature a great deal. The dose was dropped to 75 grains a day; the temperature was going up, but the joints were not clearing up. Then the dose was increased, as you have to do occasionally, up to 200 grains a day before we began to affect the patient's condition favorably. Again toxic

symptoms appeared and we had to drop the drug for two days, and then again went back to 200 grains, and by manipulating in that way finally the fever came down and the joints cleared up. Now the salicylates were continued at 50 grains a day for another week or two and then the patient was allowed to go home. In one week's time he began to have polyarthritis again and came back to the hospital with general polyarthritis, and we had to go through the whole procedure again, but this time, instead of doing what we did before, allowing the man to go out while still under the influence of 50 to 75 grains a day, the drug was tapered off. It was given in the form of aspirin and tapered off as you see here, and this time the patient recovered and remained well. So that is a better way to treat the patient than merely to clear up his symptoms and let him go.

Now just a little general outline of what we do for these patients. The specific action of the drug and how to handle the patients with salicylic acid. I hope I have made these points clear enough so that you will appreciate the different types of response and what to do. Now the general treatment plan. Of course, all patients should be quiet in bed until free from fever. In every case with visceral complications from the heart the patient should remain in bed until the cardiac rate is normal or practically normal. Then as soon as you get them up I think it is well to begin massage; it is very grateful to patients who have been in bed for a long time to have the joints and the muscles massaged. Passive massage is a form of exercise that does not throw much work on the heart and yet improves the general muscle tone. Patients do get up and about in better condition when they have been massaged. The food for these patients should be made attractive and enough given to satisfy them. They ought to have at least 3000 calories a day, if not more, because rheumatic fever is one condition that leaves your patient emaciated and anemic, and you want to save his strength as much as possible. As for bedclothes: a little point worth mentioning is that since these patients usually sweat a great deal, if you use flannel or cotton flannel sheets and night clothes when they sweat they are not left in a wet muslin poultice, as is the case

with those patients who have nothing but muslin or linen next their skin. It is very essential to care for the skin properly. These patients sweat so much that they require frequent bathing carefully performed because of pain, and it is well to use powder rather freely. The position of the patient in bed is more or less important. A very sick rheumatic fever patient rests most easily in the position one gets in the Gatch bed, sitting up with the legs raised. Sitting up relieves the legs a great deal and this is the position of least exertion. If you cannot obtain the Gatch bed, your patient should have a back-rest, while pillows beneath the knees and arms also relieve them a great deal. Binding of the joints with cotton is a very agreeable detail that the nurses have worked out here. They take 1 inch or 1½ inches of cotton, cover it with gauze and make a huge binder which goes around the joint and laps over, and is pinned with safety-pins. This bandage splints the joints and keeps them warm, and if you want to use local applications you don't have to take it off each time; you just lay the binder back on the bed and expose the joint for inspection and then put it up again with the least inconvenience and pain to the patient.

I think I have called your attention to the medication. With the salicylates we always combine a proportionate amount of sodium bicarbonate, so that if the patient is getting 120 grains of sodium salicylate he is also getting 240 grains of sodium bicarbonate. This is a general rule worked out empirically and one which seems to work well. If the sodium bicarbonate is repulsive to the patient, as it is to many, you may decrease the drug. What we usually do is to give ten doses of the drug a day; we don't give it during the night. If we want to give 150 grains a day, we give it in ten doses. Then, as you decrease the drug, you can decrease the interval and decrease the amount each time. It is said that pleural exudates disappear under the use of salicylates just the same as joint exudates. Occasionally you have to tap the pleura, as you do in any pleurisy with effusion. Another expression of rheumatic fever is hyperpyrexia—that is the form of rheumatic fever where the temperature goes up to 108° or 109° F.; you see this but rarely nowadays. These patients

get no salicylates. In this hyperpyrexic form of rheumatic fever you have to treat the patients with cold baths just as in hyperpyrexia from any other cause. In giving salicylates, the points you should look out for are first, nausea, then ringing in the ears. Occasionally patients develop delirium, and this delirium can be the most troublesome thing in medicine. Patients I have seen with salicylate delirium had the most acute mania you could possibly imagine. You have to treat these patients as you would acute maniacs; you have to use morphin, while at times the administration of paraldehyd is useful. Certainly you have to withdraw the salicylate, and when you start in again you have to proceed most cautiously and it is well to give it in some other form. The patients with general cardiac symptoms or symptoms of cardiac involvement should remain in bed from six weeks to two months. That is one of the hardest things you have to do in medicine, namely, to keep in bed these patients who feel perfectly well, and to emphasize how important rest is for them without making them hypochondriacs. And that is a thing that requires not only knowledge, but skill in handling patients. Some you will have to scold, others you have to coax; and to apply the right psychic therapy is almost as important as to apply the right drug, so that the treatment of this disease should be directed not only toward polyarthritis, but toward what is a more serious symptom, the cardiac involvement, that is, pancarditis.

CLINIC OF DR. WALTER W. PALMER

PRESBYTERIAN HOSPITAL

ACIDOSIS; TWO CASES OF DIABETES MELLITUS AND ONE CASE OF CHRONIC NEPHRITIS WITH SEVERE ACIDOSIS

Methods for Determining the Condition of Acidosis. The Use of Sodium Bicarbonate in Combating this Condition.

THIS afternoon, gentlemen, I propose to show you 3 cases illustrative of the condition of acidosis. The cases themselves need occupy but little of our time, but I wish to take this opportunity to present for your consideration in as simple a manner as possible certain fundamental facts concerning acidosis, a clear understanding of which is necessary to determine the etiology, diagnosis, and intelligent treatment of this condition.

CASE 1.—Miss M., aged twenty-nine, is an American schoolteacher, with a history of diabetes of some five years' duration, the onset of which she associates with a broken arm. An interesting feature of her family history is that her mother died at the age of thirty-seven of diabetes mellitus. One year after onset she was "in a stuporous condition for seven days." During the past four years she has been under excellent care. Her treatment has been prolonged low diets and occasional fasts to get rid of the last trace of glycosuria, which has resulted in keeping her sugar free, for most of the time in good condition, and in her ability to do considerable work. For the past few months it has been necessary for her to keep to a very low diet in order to remain free from glycosuria. Four months ago she decided to break away from her diet and to eat enough to make

her comfortable. According to her statements she has been eating practically everything except that she has made an attempt to keep the fats low. Also she has discontinued testing her urine for sugar. Two weeks ago she developed marked edema of the legs and abdomen, but this disappeared promptly following the ingestion of 16 grams of theocin. Since then she has grown rapidly weaker and had increasing difficulty in shortness of breath. For two days she has spent most of the time lying down. Yesterday she was nauseated and vomited. Appreciating her condition, she took two teaspoonfuls of sodium bicarbonate. She has eaten nothing for the past two days, partly because of her lack of appetite, and partly for treatment of the acidosis, which she recognized herself. We shall see the patient for a moment.

She is well nourished, although apparently very weak. Notice the deep dusky flush on both cheeks. A very striking feature is the drowsiness and intense hyperpnea. You observe the deep breathing, with no pauses between respirations. At the end of each expiration is a soft sigh. The rate is not so rapid as one is at first led to believe. It is quite different from the breathing one sees in pneumonia, which is short, rapid, and shallow, followed by the characteristic expiratory grunt. Nor does it simulate in any way the breathlessness encountered in heart disease or the extremely rapid respiration occasionally seen in hysteria. If we speak to Miss M. she partially opens her eyes, answers languidly, but intelligently. The lips are dry, the tongue red. The type of breathing, known as Kussmaul breathing, and the picture you have just witnessed is as perfect as you will often see. It was very carefully and accurately described as "diabetic coma" by Kussmaul in 1873, whose original description I strongly urge you to read.

There are certain laboratory findings which I shall give now, but reserve the discussion of them, as also the etiology, diagnosis, and treatment until after showing the other cases and taking up the subject of acidosis in general.

The urine contains 0.6 per cent. sugar and a heavy trace of albumin, with many highly refractile casts. These casts have

long been termed "coma casts." It also contains diacetic acid ++++ and acetone ++++ reactions. The twenty-four-hour amount of urine contains 6.2 grams ammonia and a total acetone of 65 grams. The blood CO_2 is 20 volume per cent.; there are 100 mgm. of acetone per 100 c.c. of blood. Blood-sugar is 0.35 per cent.

Case 2.—Mrs. L., aged fifty-one, born in Germany, is a widow, who has known that she had diabetes for three years, but on a restricted diet has been comfortable, attending to her daily duties as a nurse. At no time has polyuria, polydipsia, or polyphagia been noticeable. She has had repeated crops of boils, which have always responded to simple treatment. Three weeks ago, however, numerous boils developed on face, neck, and back, several of which have become very large, painful, red, and swollen. She entered the hospital twelve days ago, at which time the boils were treated surgically by incision and drainage. At that time her urine contained 2.5 per cent. glucose, acetone ++++, and diacetic acid ++++ reactions; no albumin, but a few hyaline casts. Blood-plasma CO_2 was 47 volume per cent. The starvation treatment was instituted. Two days later the blood CO_2 was 40 volume per cent. The starvation treatment of the diabetes has been continued until today, a period of eleven days, with very little change in the glycosuria, but with diminishing acetone and diacetic reactions in the urine. The blood-plasma CO_2, however, shows a constant diminution, until today it is 28 volume per cent.

As you see, Mrs. L. lies comfortably on her back, with the elaborate surgical apparatus all about for the purpose of irrigating the incised boils with Dakin's solution. There is a bright red spot on each cheek. She is breathing just a little more deeply than one would expect, with only a slight pause between respirations, but no sighing. The respiration suggests the type we have just seen, but is far less marked. There is apparent drowsiness, but the eyes are open and a general interest is expressed in all that is going on.

Case 3.—This case is one of advanced chronic nephritis. Mr. M., aged forty-four, American by birth, is a lawyer, who

for the past eight months has been troubled with general weakness, dyspnea, swelling of the feet and ankles, sleeplessness, faulty vision, nausea, and occasional vomiting.

We notice a gray-haired man with pallid complexion, puffiness under the eyes, expressionless face, and lips with a slight purplish hue. His breathing is labored, deep, suggesting air hunger, in severity occupying a position about midway between the first and second cases. His breath has a very foul, urinous odor. He is particularly restless, tossing from side to side on the bed.

On physical examination one finds a large heart beating about 100 times to the minute at a regular rate. The arterial walls are thickened and tortuous. The tension seems increased, the blood-pressure is 180 systolic, 120 diastolic. At the bases of the lungs posteriorly are numerous moist râles. A moderate edema of the lower legs is evident.

The urine has a specific gravity of 1006, heavy trace of albumin, many hyaline and granular casts. The tests for acetone, diacetic acid, and sugar are negative. The twenty-four-hour amount of ammonia in the urine is 0.3 gm. On entrance about four weeks ago the urea index was 3.7, blood urea at this time 1.119 gm. per liter. Three days ago the urea index was 0.7; the blood urea 3.0 gm. per liter. In two hours no phenolsulphonephthalein appeared in the urine. Today the urea index is 0.17, and the blood urea 3.9 gm. per liter; blood-plasma CO_2 20 volume per cent.

The last case you have seen is an advanced chronic nephritis with the clinical picture of severe acidosis. Evidence of acidosis is found in the blood CO_2, which is only 20 volume per cent. The cases just shown represent very severe and serious grades of acidosis. Equally severe conditions occur in gastro-intestinal and nutritional disturbances of children, a description of which is given by Marriott and Howland. Varying milder degrees of acidosis occur in many other pathologic conditions, as in the acute infections and chronic diseases.

Discussion.—To diagnose and treat the condition of acidosis intelligently we must know in some detail about the reaction of the body in general, the constancy of this reaction, and how it is

maintained. Life and proper functional activity of the cells in the body depend to a great extent on the maintenance within quite narrow limits of three important factors, namely, temperature, osmotic pressure, and reaction. The mechanism by which the organism is able to keep the reaction or acid base equilibrium constant under the stress and strain of metabolism and muscular work is quite well known; less is known about the regulation of temperature and osmotic pressure. I think it is safe to assume that all of you have heard the expression *Hydrogen-ion concentration* and its use in connection with the blood. What do we mean by the hydrogen ion concentration of the blood? Pure water, H_2O, ionizes as follows: $H_2O = \overset{+}{H} + \overline{OH}$, *i. e.*, very few molecules separate into H and OH-ions in equal numbers. In pure water at 25° C. there is 1 gm. of ionized H in 10,000,000 liters. This is taken as the standard of neutrality. In other words, when the concentration of H-ions in any solution is greater than the concentration of OH-ions, or greater than 1 gm. in 10,000,000 liters, the solution is acid, and conversely, when the concentration of H-ions is less than the concentration of OH-ions or less than 1 gm. in 10,000,000 liters, the solution is alkaline. Normal blood and body fluids as found in the body contain about 0.4 gm. of ionized hydrogen in 10,000,000 liters, and by our definition are slightly alkaline. The concentration of H-ions in the blood may not vary during life except within extraordinarily narrow limits. This is better appreciated when I tell you that an increase to the amount of 1 gm. in 10,000,000 liters promptly results in death.

Next, how does the body maintain this very constant reaction throughout life? As the result of metabolism there are constantly being poured into the blood-stream and body fluids varying amounts of acid substances which would soon change the slightly alkaline blood to an acid medium were it not for a special protective mechanism. Among the important constituents in the blood-plasma which maintain the reaction at a constant level are sodium bicarbonate, phosphates, and albumin. This afternoon I shall consider the part played by the bicarbonate only, for the simple reason that it is by far the most important factor.

Perhaps the manner in which the blood keeps from becoming acid may best be explained by a rather crude illustration. For the moment let us consider the blood as partially filling a receptacle similar to the one I have placed on the board (Fig. 48). The space over the blood we may represent as the lungs, and the outlet at the bottom the kidneys. Under normal conditions the concentraton of sodium bicarbonate in the blood is kept at a very constant level, which we may designate by the line *b* in the diagram. Now, if either through a special diet, or by the administration of sodium bicarbonate, this level is raised, the kidney, so sensitive to the slightest changes, removes the excess and returns the blood bicarbonate to its normal concentration level. As alkaline excess in the organism occurs quite infrequently unless artificially produced, the fate of the acids becomes of greater importance.

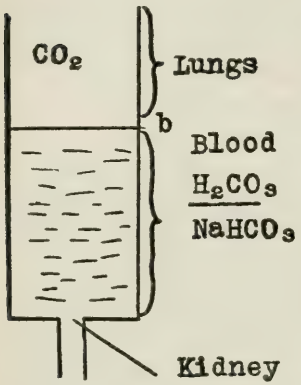


Fig. 48.

The first acid factor to consider is CO_2. A very important property of sodium bicarbonate enables the blood to take up and transport to the lungs large amounts of carbonic acid, which are being produced constantly. In the blood carbonic acid and sodium bicarbonate are associated in very definite proportions, determined by the reaction (hydrogen-ion concentration) of the blood, actually about 1 part of CO_2 to 12 parts of sodium bicarbonate. It is necessary that they occur in these proportions constantly, otherwise an excess of carbonic acid would increase hydrogen-ion concentration of the blood beyond that compatible with life. This increases the carrying power of the blood for this product of metabolism and is of great importance to the body.

As the blood comes to the lungs, in obedience to the law of partial pressure, CO_2 diffuses into the alveoli to be discharged from the body during respiration and the blood made ready to take up more carbonic acid. It may not be out of place to say

here that the center in the medulla which controls respiration is exquisitely sensitive to very slight changes in the reaction of the blood caused by increased carbonic acid. So sensitive is it that when the concentration of H-ions increases over the normal of approximately 0.4 to 0.406 gm. in 10,000,000 liters, the respiratory mechanism is stimulated to act. It is this very slight change going on constantly that produces regular respiration. You may demonstrate this phenomenon to your own satisfaction by a simple breathing experiment. As you breathe the air from the lungs over and over again into an air-tight bag and the concentration of CO_2 increases you find your respirations are increasing from say 20 to 40 in a very short time. Diffusion of CO_2 from the blood into the lungs takes place with great ease. The factor of safety is very great.

Besides CO_2, other acids which are not volatile are produced during metabolism, for example, hydrochloric acid, sulphuric acid, phosphoric acid, oxalic acid, beta-hydroxybutyric acid, diacetic acid, lactic acid, and other organic acids. Strong acids, like hydrochloric acid and sulphuric acid and oxalic acid, immediately on their production claim base and form neutral salts. Other acids produced, such as phosphoric acid and beta-hydrooxybutyric acid, also claim base, but through a quite remarkable and, indeed, fortunate mechanism in the kidney may be excreted to a considerable extent in the free state, thus saving for the body base for use over and over again. Bases so returned, of course, in the presence of abundant CO_2 form bicarbonate, thereby helping to keep the concentration of this substance at a proper level. On inquiry in a little more detail just how this occurs let us refer to our simple diagram on the board. Imagine for the moment that there are many small inlets on the side of the receptacle which are pouring acid substances into the blood sodium bicarbonate solution. The acid radicles claim base immediately. The base kept on hand for such purposes is that combined with the bicarbonate, and in our illustration is sodium. The CO_2 being replaced by some other stronger acid radicle is liberated to the blood-stream and eventually eliminated by the way of the lungs. I chose sodium to combine with the bicarbonate ($—HCO_3$)

because it is probably the most important inorganic ion in this connection. Another extremely fortunate circumstance arises. One of the waste products of protein metabolism is urea, which you will remember is composed of NH_3 and CO_2. But when there are large amounts of acid being produced the ammonia is used to neutralize these acids, and as we know the CO_2 is easily eliminated by way of the lungs. The neutral ammonium salts of the acids which do not appreciably affect the reaction of the blood are then excreted by the kidney, another illustration of a protective mechanism.

Under ordinary and usual circumstances the amount of base ingested in the food, the utilization of ammonia and the ability of the kidney to save base for the body, keep the bicarbonate in the blood and body tissues at a very constant level. If, however, acids are produced to such an extent that this mechanism fails to take out for the body and blood all the acid products, then the bicarbonate base of the blood is called upon and eliminated in combination with the excess of acid radicles. This leads to a lowering of the bicarbonate in the blood and a condition known quite generally as acidosis. A condition of acidosis may result also in cases when the acid radicles combine with the bicarbonate base and are not eliminated. The available base is diminished. The diminished bicarbonate in the blood reduces the carrying power of the blood for CO_2, which theoretically may lead to a damming back of CO_2 in the tissues. A third condition of acidosis may exist with the bicarbonate of the blood at a normal level. This is accomplished when the respiratory center does not respond to the usual slight change in H-ion concentration which is controlled by the ratio, $\frac{H_2CO_3}{NaHCO_3}$, but requires a slightly greater H-ion concentration than normal, thereby producing an accumulation of CO_2 in the blood. This condition is known as CO_2 acidosis. For our definition, then, with the exception of CO_2 acidosis, we may consider acidosis as a condition in which the concentration of bicarbonate in the blood is reduced below the normal level.

Demonstration.—The property of the blood to neutralize acids and alkalies without changing its reaction very appreciably

may be demonstrated quite simply. Here are four beakers, two of which contain a few cubic centimeters of a solution of phosphates (1 part monosodium phosphate to 5 parts of dibasic phosphate), having in general the reaction and property of the blood carbonates. Two of the beakers contain normal salt solution. On adding phenolphthalein to one of the beakers with the phosphate solution no color is produced. In other words, it is acid to phenolphthalein. To the other phosphate solution we add methyl orange, which produces a yellow color, thereby demonstrating that the solution is alkaline to this indicator. Similar results are obtained in the beaker with salt solution. I have here a quantity of sodium hydroxide of about $\frac{1}{10}$ normal strength. On adding 1 drop to the salt solution with the phenolphthalein the color immediately becomes a deep pink, indicating alkalinity. But when added to the phosphate solution several cubic centimeters are necessary before any pink appears, and then it is very faint. Several more cubic centimeters are necessary before the deep pink of the salt solution is reached. Now, taking some HCl solution of about $\frac{1}{10}$ normal strength, we add 1 drop to the salt solution containing methyl orange. A deep red results, indicating marked acidity, but several cubic centimeters are necessary to produce a light red when added to the phosphate solution. This serves as a striking illustration of the protective power of the blood against alkali and acid. We are now in a position to consider the etiology, diagnosis, and treatment of acidosis in our cases. It will be necessary first to consider methods for determining the condition of acidosis.

It is quite evident from our discussion that in order to make a diagnosis of acidosis some method of estimating the concentration of sodium bicarbonate in the blood either directly or indirectly is necessary. Although this is not the time nor the place to discuss laboratory metods in detail, I shall call attention to a very simple device for determining approximately whether the concentration of sodium bicarbonate in the blood is at a normal level. You will remember in our discussion of the regulation of the acid base equilibrium of the body that if alkali in excess of

that needed in the blood were ingested the kidney promptly eliminated it. This fact is made use of in the following manner: If 5 gm. of sodium bicarbonate are taken by mouth by normal individuals the urine shows the effect within an hour by marked reduction of its acidity. In pathologic cases, however, when the level of the blood bicarbonate is below normal, increasing amounts are necessary to affect the acidity of the urine—*i. e.*, not until the normal level of bicarbonate is restored will there be any effect on urine acidity. Testing the reaction of the urine after sodium bicarbonate serves two purposes: first, it gives information regarding the degree of acidity; second, it indicates the proper amount to give in a therapeutic way, for after you have restored the level of bicarbonate to normal then you have accomplished all that you may expect by the administration of alkali. Furthermore, it is very inadvisable to push the administration of alkali beyond this point, as disturbing gastro-intestinal symptoms and headache frequently appear. Also if the reaction of the urine is pushed to an extreme degree of akalinity, albuminuria may be produced. An objection to the above method exists, because a false impression of the degree of acidity present may be gained when the kidney is damaged or does not react normally to alkali excess in the blood.

You remember that CO_2 in the blood exists in a certain definite ratio to the amount of bicarbonate present, and in obedience to the law of partial pressures diffuses into the alveoli of the lungs. Now if there has been a drain on the blood bicarbonate sufficient to reduce it below the normal level, the amount of CO_2 in the blood will be lowered. By making a forced expiration into a long tube and taking a sample of the very last air forced out of the lungs, the precentage of CO_2 may be estimated. This is done by taking a measured amount of the expired air into a gas buret, absorbing the CO_2 in it by means of sodium hydroxid, noting the difference, whence the percentage is easily calculated. Normally, CO_2 in expired air is between 4.6 and 5.8 per cent., or, as more frequently expressed, 35 and 44 mm. tension. The methods of Fridericia and Haldane are those in common use.

The most accurate method is, of course, to estimate the actual amount of bicarbonate in the blood. Recently Van Slyke has devised an apparatus making this possible in a comparatively simple manner. The blood-plasma is introduced into a chamber provided with a small gas buret, acid is added to free the CO_2, which is bound as sodium bicarbonate, gains liberty by extraction *in vacuo*, and finally is measured in the small buret. Normally, 100 c.c. of blood contains 55 to 65 c.c. of CO_2 gas bound as bicarbonate. The determination of alveolar air, CO_2, and blood bicarbonate needs a certain amount of laboratory training and experience; therefore it would be wasting your time to give detailed description of the methods. Their usefulness may, however, excite the curiosity of some of you to acquire the technic necessary for these procedures.

It is now possible to discuss the etiology, diagnosis, and treatment of the conditions illustrated by the cases. In Case I the urine and blood reveal large quantities of acetone bodies which, as you know, appear distributed in varying amounts between beta-hydroxybutyric acid, diacetic acid, and acetone. The presence of these bodies is evidence of faulty or incomplete oxidation of the fats. Normally, these bodies exist in the merest traces in both urine and blood. The blood of Miss M. contains 100 mgm. of total acetone in 100 c.c. and the urine contains 65 gm. of acetone in the twenty-four-hour amount. If one-half of the latter amount be present in the form of beta-hydroxybutyric acid, then 58 gm. of the acid or nearly 6 liters of $\frac{1}{10}$ normal acid solution were eliminated by the kidney. Normally, there is seldom over 1 liter of $\frac{1}{10}$ normal acid in the twenty-four-hour urine when the monobasic and dibasic phosphate radicles are considered. We may say with certainty, I think, that beta-hydroxybutyric acid is largely responsible for the condition of acidosis existing in the case of Miss M. The steps leading up to the discovery of beta-hydroxybutyric acid as the cause of acidosis in diabetes may interest you. In 1877 Walter introduced HCl into the stomach of rabbits, thereby producing a condition of collapse and unconsciousness with dyspnea resembling the Kussmaul diabetic type. He observed a marked increase in

ammonia excretion, also a great reduction of the blood CO_2. Furthermore, he was able to protect the rabbits by giving subcutaneous injections of sodium bicarbonate, so that three times the fatal dose of HCl could be injected into the stomach. When an animal which has received the fatal dose of acid is practically dead, with both heart and respiration stopped, intravenous injection of alkali brings back life, heart and respiration both start again. With Walter's work in mind, Stadelmann, a pupil of Naunyn, in 1883 proposed a theory of acid poisoning as the cause of coma and increased ammonia excretion in diabetes. At the same time he suggested the treatment of this condition by means of an alkali. By determining known basic and acid radicles Stadelmann estimated that considerable amounts of unknown acid must be excreted in these cases, for he found the basic radicles far in excess of the known acid radicles. Working on the theory that this was probably an organic acid, at that time unknown, he isolated and identified crotonic acid, which results from heating beta-hydroxybutyric acid and sulphuric acid under certain conditions. It remained for Külz and Minowski a year later to isolate and identify beta-hydroxybutyric acid.

The diagnosis of a condition of acidosis in this case rests on the finding of a very low plasma CO_2, 20 volume per cent. (normal 55–65 volume per cent.). The large amounts of ammonia, 6 gm. in twenty-four hours, serves as confirmatory evidence.

How shall we treat the condition we have here? The points which have to be decided are, first, shall we give food? Second, shall alkali be used? In regard to food, let me say that during starvation the patient has become rapidly worse. The acidosis has increased, so the only course, it seems to me, is to give food. This should be done in small amounts, chiefly in the form of protein, as, for example, eggs and fat-freee milk. Alkali certainly is indicated. Sodium bicarbonate is the drug of choice. The manner of administration is important. She should receive 5 gm. in 100 c.c. of water by mouth every hour. At the slightest indication of nausea or discomfort following the ingestion of soda the drug should be discontinued, and if the blood bicar-

bonate remains low, recourse to intravenous injection is next in order. It is best to give 250 c.c. of a 3 per cent. solution of sodium bicarbonate at intervals of three or four hours. The intravenous injection of large amounts, say 1000 c.c. or more, of a soda solution is not infrequently attended by disastrous results. I refer to sudden death during or just after such injections. The administration of alkali should also be controlled by frequent blood CO_2 determinations if possible, or in any case by watching the reaction of the urine. The first effect of the alkali to be found in the urine is a reduction of the ammonia. The patient should be encouraged to take large amounts of fluid with the view of enabling the kidney to eliminate large amounts of the abnormal acid. We know that the kidney will not excrete beta-hydroxybutyric acid, in a concentration greater than 1 per cent. I may say that the outlook in cases as severe as this is extremely dubious.

The situation in the second case, Mrs. L., is quite different from the first, Miss M. Although during the eleven days' fast the acetone bodies have diminished in amount, there has been a constant drain on the blood bicarbonate until the low value of 28 volume per cent. has been reached. The mechanism for maintaining the blood bicarbonate at a constant level has proved inadequate and it has been necessary to call upon the bicarbonate base itself to help out. We have illustrated here a quite different condition than exists in Case 1. No large amounts of acid substances are being produced. Occasionally large amounts of acetone bodies accumulate in the blood, which accounts for the condition of acidosis. In contrast to this case not infrequently one sees individuals in which prolonged fasting results in an increase in the blood bicarbonate. Further study of the two phases is necessary before we shall be able to offer any satisfactory explanation as to why one should benefit and others be injured by this treatment.

Two considerations are of importance in the treatment of Mrs. L.: First, diet; second, use of alkali. As eleven days' fasting has not improved the glycosuria and the concentration of sodium bicarbonate in the blood has constantly diminished,

in spite of the fact that beta-hydroxybutyric acid and diacetic acid in the urine have decreased, the desirability of giving food seems to be clear. Both food and alkali are to be given as described in the previous case.

Case 3.—Nearly as severe symptoms as appeared in our first case exist in the last case I showed you. Instead of diabetes, however, the diagnosis of chronic nephritis with uremia seemed established beyond a doubt. There is also a severe acidosis present, as shown by the blood bicarbonate determination, which reveals only 20 volume per cent. What is the nature of the acidosis in this case? The damaged kidney fails to excrete the acid products as fast as they are formed. Also this type of kidney is denied the full use of ammonia to excrete acid radicles. Here we have then an acidosis due largely to the retention of phosphates. An increase in the phosphates in the blood in these cases may also be demonstrated. As much as five times the normal amount is not infrequently found. Unfortunately, the amounts of phosphates in the blood of this patient have not been estimated. What form of treatment is available? There is little we can do. The damaged kidney is no longer able to do its work. Temporary relief may be secured by the use of sodium bicarbonate, but such relief is of doubtful value in cases of this kind. If alkali is given, it should be carefully controlled. It has been shown recently that the damaged kidney does not maintain the blood bicarbonate level so easily or so constantly as the normal kidney. In one of my cases the ingestion by mouth of 30 gm. of soda was followed by a rise in the level of blood CO_2 to 104 volume per cent. Although the kidney at this time was elaborating a urine more acid than blood, it is clear that a marked alteration in the osmotic pressure of the blood may prove more serious than the original acidosis.

In addition to the attempt in this clinic to make clear in a very simple way the mechanism for the regulation of the acid base equilibrium in the body, I have tried to impress you with two facts of importance, first, the condition of acidosis may be easily determined, and, second, that sodium bicarbonate is a most useful and valuable drug in combating this condition

when used properly and intelligently. I have tried to explain to you how this may be done, and if my effects have met with success the exercise has not been in vain.

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CLINIC OF DR. WALTER A. BASTEDO

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MUCOUS COLITIS

Occurrence, Character of Stools, Pathology, Diagnosis, Symptoms and Associated Conditions (Constipation, Intestinal Putrefaction, Colic, Stomach Derangements, Tetany, Bronchial Asthma, Hay-fever, Urticaria, Angioneurotic Edema, Ecchymoses, Neuroses with Fatigability), Prognosis, Treatment.

Mucous colitis (colica mucosa) is a condition characterized by the formation in the large bowel and the expulsion at irregular intervals of large quantities of mucus of abnormal character. Whether it is a disease entity or only a symptom is impossible to say. It occurs in both sexes and at any period of life from infancy to old age, and, contrary to the general belief, is of frequent occurrence in men. It may be only incidental to other lesions and of relative unimportance in the clinical picture, or it may be a cause of, or a dominant factor in, profound disturbances of the health. It sends the patient for medical aid, not usually for the mucous discharge unless this is mistaken for worms, but rather for some accompanying manifestation such as persistent constipation, abdominal pain, flatulence, headache, or lack of physical or mental vigor and endurance. Strangely enough, patients frequently fail to speak of even marked mucous stools unless interrogated by the physician.

It has been a commonly accepted dictum that the clinical syndrome, mucous colitis, included always three features, viz., constipation, colic, and nervousness, but the disease exists in harmful form without any of these conditions. It has also been assumed that there is always an underlying status neuroticus,

but the fact that with adequate treatment of the colitis a severe neurosis not infrequently disappears and leaves the patient not any more nervous than other people would suggest that the colitis, at least in these instances, is not a result of a neurotic state.

The only distinguishing feature, therefore, is the passage at irregular intervals of large quantities of mucus.

The Stools.—The discharged mucus may be soft and translucent and apparently freshly secreted, and if mixed with the feces may not be very obvious till the feces are washed in a stool sieve. This is the character of mucus in mild cases or cases approaching a cure.

But more frequently the mucus is dried out or coagulated, so that it forms a membrane and appears in plaques, shreds, strings, skins, or casts. Its membranous nature may not be obvious until a piece is floated out in water. The strings are often taken for worms; they may reach as much as 2 or 3 feet in length. The mucus is not accompanied to any great degree by other elements of inflammation, but the drier pieces may bear bloody spots like scabs, as if torn off forcibly from an inflamed membrane.

Besides mucus, the stools may contain intestinal sand and blood. *Intestinal sand* occurs in large amounts in some cases. It is composed mainly of calcium phosphate, is hard and gritty, and is capable of severely irritating the colon, rectum, and anus. *Blood*, occult or visible, has been present in the mucus of a number of my cases, though only those pieces of mucus with a brownish color have been tested. Mummery reports its presence in the stools in 60 per cent.

Pathology.—There is nearly always some degree of chronic colitis, this varying from a very slight inflammation of the mucous membrane to an extensive diseased area, or a badly cicatrized condition following dysentery. It probably favors absorption of intestinal poisons. In addition, in many patients there is laxity of the abdominopelvic walls, with general visceroptosis and falling of the kidney, especially that of the right side, or ptosis of the proximal portion of the colon with movable cecum. There may also be other conditions which affect the alimentary tract directly or reflexly, as redundant colon, megacolon, chronic

appendicitis, cholelithiasis, ulcer, carcinoma, pelvic inflammations, etc. As a rule, some portion of the bowel is found in a spastic state, and this is usually the descending colon or sigmoid flexure. With this is frequently found an atony of the cecum and ascending colon, with distention and great thinness of the wall. This atony is in some instances incurable because of a failure of innervation, *i. e.*, absence of Auerbach's plexus, or because of serious destructive lesions of the mucous membrane. Absence of bile has been held by some as the cause of the condition, but in many of our cases the reaction for urobilin in the stool has been strongly positive.

Diagnosis.—This rests (*a*) on the history of the occurrence of stools of practically pure mucus, or of the appearance of the characteristic strings or casts in the stools; (*b*) on the finding of the strings or casts or abundant mucus in a specimen submitted by the patient; (*c*) on observation through a sigmoidoscope of a dry rectal or sigmoidal mucous membrane with tenacious mucus clinging to its wall; (*d*) on the finding of the characteristic strings or large quantities of mucus after a dose of castor oil or a test colonic irrigation. If mucous colitis is sought for only when there is colic many cases will be overlooked.

Symptoms and Associated Conditions.—*Constipation.*—This is a usual accompaniment of mucous colitis and must be sought for even though the bowels move daily. For constipation is not a condition of infrequent defecation, but of insufficient or retarded defecation. In these cases there is often a persistent retardation in the cecum in spite of daily stools or the passage of small fragments several times a day (a seeming diarrhea). Colonic lavage has shown that marked stagnation may exist though the bowels seem freely open. The relief of intestinal stasis is essential in the cure, but does not alone bring about a cure. In many of these cases the cecal wall is thin and atonic, there is splanchnoptosis, and the abdominal walls are flabby, so that intestinal stasis is pronounced. As in women this causes pressure on the pelvic organs, many of these women seek and get gynecologic treatment. (Occasionally with the colic attack there is a violent diarrhea with foul-smelling stools.)

Intestinal Putrefactive Toxemia.—Without doubt, the neurotic manifestations and the condition of mental and physical fatigability may in many instances be traced directly to a chronic toxemia caused by the absorption of chemical substances formed in the bowel. And it is probable not only that the constipated bowel of mucous colitis favors bacterial proteolysis, but also that the damaged mucous membrane promotes the absorption of deleterious material. The subject of intestinal toxemia is too large to be dealt with here, but it is important to remember that quite often the treatment of mucous colitis involves extensive consideration of the associated toxemia.

Abdominal Pain.—This is present in less than half the cases. It may consist of soreness in any part of the abdomen; but more striking are attacks of severe colic or cramps which may show in any part of the colon from cecum to sigmoid flexure. The attack is regularly preceded by a period of constipation.

The cramps come on in paroxysms (most frequently at night), and if success is not obtained in the expulsion of the mucus, may recur a day or a week later. They are prone to change their position, but have at times been localized to such an extent that they have simulated acute surgical conditions; indeed, in many instances they have been responsible for abdominal section performed under the diagnosis of appendicitis, gall-stones, stone in the ureter, acute obstruction of the bowels, or duodenal or other perforation. However, as a rule, the character of the cramp may be recognized, for it is not associated with fever above 100° F., or a leukocytosis; it is accompanied by a state of great nervous tension, it is prone to change its site and move along the colon, and it is relieved by a free evacuation of mucus from the bowels. Persistence of mild cramps or soreness has also been the cause of many exploratory laparotomies for chronic conditions.

These patients feel pain very keenly and are prone to be highly neurotic at the time of the attack, hence may writhe or scream with the colicky pain, and implore the physician to give relief. The condition in these colic attacks has been compared with that in bronchial asthma, in which there is great nervous-

ness, muscular spasm, and a collection of thick, tenacious mucus. Some of my cases have had both conditions.

Causes of Colic.—As the colic is sometimes associated with angioneurotic edema or urticaria, it has been postulated that the intestinal attack may be due to a localized visceral edema, and it is quite possible that this is the case in some instances. But I know of no proof that this is so.

The evidence would indicate that, as a rule, the colic is the result of the attempt of the bowel to expel clinging mucus. This mucus, acting as an irritant, induces spasmodic contraction of a portion of the intestine, and undoubtedly at times is gripped at the point of spasm, or sticks so tightly to the mucous membrane that it cannot be loosened. But the spasmodic part of the bowel is not the pain-producing portion, for, as shown by A. F. Hertz, not contraction, but distention, of the bowel is the cause of pain. Thus the pain comes from the increased pressure in and consequent forcible distention of the portion of the gut above the contraction; and the distention is produced by the material and gas brought down by peristaltic waves made highly active by an endeavor to force the obstruction. The pain ceases if the peristalsis is strong enough to overcome the spasm. The spasm probably occurs not with the soft, readily passed mucus, but only when the mucus has been retained until it is desiccated or coagulated so that it acts as a mechanical irritant.

The tenacity with which this kind of mucus clings to the mucous membrane is remarkable. It is with difficulty removed even with forceps, and von Noorden has been "able to determine at autopsy that the mucus may be so tightly adherent to the bowel wall that it cannot be removed with a strong stream of water that is allowed to play directly upon it from a hydrant." It is well to remember, however, because of our use of colon lavage in the treatment, that the mucus *in situ* can probably be softened and loosened by prolonged soaking in water.

Stomach Derangements.—To overlook these is to fail in the treatment. The most frequent derangements of the stomach are achylia, myasthenia or atony, and hyperacidity. They make decided modifications in the required diet. A phenomenon

usually associated with gastric atony and observed by me in a few cases is *tetany*.

Bronchial Asthma, Hay-fever, Urticaria, Angioneurotic Edema.—In a number of *asthma* cases referred to me the attacks have been directly associated with mucous colitis and intestinal toxemia, and the asthma has resisted the ordinary remedies until a decided change in the bowel state has been obtained. In *hay-fever* cases I have seen those who have or have had mucous colitis with colicky attacks occurring at other times of the year than the hay-fever season, but worse during the hay-fever attack; and I have seen occasional lessening of the hay-fever symptoms as the result of the treatment for mucous colitis. I can recall two hay-fever patients that were sensitive to a wide range of proteins, whether of pollens or of animal flesh, eggs, beans, or even milk, either when applied intracutaneously or when taken by mouth. Both had mucous colitis and became definitely less sensitive to protein foods as the colitis yielded to treatment. *Urticaria* is an occasional recurrent or persistent manifestation, as also is *angioneurotic edema*, which appears especially about the face, but also in other parts of the body.

These complications suggest protein sensitization and the possibility that there is absorption of unchanged protein in minute amount through the diseased mucous membrane of the bowel, with mild anaphylactic results. It is thought by some that an angioneurotic edema occurs in the intestines and is the cause of colic; and under such a title as "The Visceral Manifestations of the Erythema Group of Skin Diseases" Osler many years ago, and Christian this year, have given instances of abdominal cramps in conjunction with urticaria, angioneurotic edema, erythema multiforme, etc. From my experience I have formed the opinion that such abdominal cramps are manifestations of mucous colitis, the skin lesions being the result of the abnormal proteolysis and intestinal absorption so often present in mucous colitis. It is well known, for instance, that histamin is at times a product of intestinal putrefaction, and that when it is absorbed it will produce urticaria. It is quite probable also

that at times minute amounts of protein are absorbed, as stated above.

Subcutaneous Hemorrhages.—I have had 2 striking cases in which highly neurotic manifestations, the formation of vast quantities of mucus in the colon, and capillary hemorrhages giving the appearance of bruises in the arms and legs have recurred from time to time. Invariably colon irrigations have been successful in checking all three conditions, the hemorrhages and neurotic manifestations disappearing with the disappearance of the membranous type of colon mucus. These cases suggest lack of calcium, but calcium in dosage of 1 to 10 gm. (15 to 150 grains) a day has had no effect whatever in checking the attacks or preventing their recurrence.

Hyperthyroidism and Hypothyroidism.—An attempt has been made to link mucous colitis with hypothyroidism, but I have seen no good result from the administration of thyroid, have seen patients unable to take thyroid, and have seen mucous colitis in well-marked cases of hyperthyroidism.

Nervous or Psychic Manifestations.—That there is a close relation between the nervous symptoms and the attacks of mucous colitis is evident, for while an upset of the bowel will result in nervousness, likewise a nervous upset will result in an attack of colitis. Just to what extent the one is causative of the other, or whether both have a joint cause, it is impossible to say, but in the treatment both must be taken into account. The nervous symptoms may take the form of mental depression, fault-finding, self-pity, irritability of temper, lack of self-reliance, inability to control others, hysteric outbreaks, and in some instances such mental instability, lack of self-control, and irresponsibility in action as to place the patient on the borderline of insanity.

Etiology.—Mucous colitis may be the sequel of dysentery or long-standing intestinal stasis, but its true origin is not known. Eppinger and Hess consider it a manifestation of vagotony, but treatment does not justify this belief.

Prognosis.—I believe that a large number of these cases can be cured, but usually only with persistence in the treatment for

a very long time. Some of them require definitely the help of surgery. Undoubtedly continued or repeated severity in the symptoms is often the result of neglect either by patient or doctor. I believe that frequently many of the neurotic manifestations disappear with the disappearance of the stringy mucus and the intestinal toxemia, leaving a patient who is no longer unduly neurotic; and I believe that the classification of the patient as a "neurasthenic" by the physician makes the outlook hopeless. I would especially deprecate such a statement as that made by a speaker at a recent meeting of the Pennsylvania State Medical Association, that "the prognosis is absolutely hopeless, the treatment is *nil*, and the sole prophylaxis would have been to sterilize the grandfather."

Treatment.—This is preventive and symptomatic. It is directed toward the prevention of the accumulation (stasis) of mucus and to the removal of the associated conditions, such as colic, constipation, intestinal toxemia, disturbed stomach conditions, flatulence, and depressed general health. We shall take up first the treatment of the abdominal pain or colic, and then the treatment of the condition after the attack of colic or when there is no colic.

1. *The treatment for the attack of colic* resolves itself into: (1) Measures to relieve pain and neurotic symptoms, and (2) measures to promote evacuation of the mucus.

(1) The first of these is attained by (*a*) rest in bed, (*b*) a large dose of bromid by mouth, (*c*) a hypodermic of atropin sulphate, 0.001 gm. (gr. $\frac{1}{65}$), with codein, 0.03 gm. (gr. $\frac{1}{2}$), and (*d*) heat, in the form of hot applications to the abdomen by hot-water bag, poultice or stupe, or a hot bath. On account of habit formation in neurotic subjects, morphin should not ordinarily be employed, but it may be where the recurrence is not frequent and the attack is very severe. For the colic the best single drug is atropin; it is of no use for the cure of the colitis.

(2) For the evacuation one may use (*a*) a large dose of castor oil by mouth—to make vigorous peristalsis. This peristalsis, beginning above the mucus, tends to separate the mucus from above downward, and, in addition, is regularly effective in over-

coming the spasmodic obstruction. (*b*) Colonic lavage with tap-water, normal saline, or a solution of sodium bicarbonate, 3j to Oj, given warm and at low pressure (2 feet). On account of the spasticity it may be impossible to get the liquid up into the colon at first, but persistence and gentleness may result in success. Irritants such as silver nitrate should not be employed in the already highly sensitive colon.

After these evacuating measures or in lieu of them in some cases, it is wise, if the attacks are very severe or persistent, to put the patient in the knee-chest position and to inject slowly into the colon ½ to 1 pint of warm olive or cottonseed oil, to be retained over night or as long as possible, a towel being placed over the anus as protection in case of leakage. Often the combination of castor oil by mouth, codein and atropin hypodermically, and the oil injection will be followed by relief and a deep sleep, with the passage a few hours later of the oil and abundance of mucus, and disappearance of the colic, with no recurrence for a long time.

2. *The treatment after the attack or in cases without colic* is designed (*a*) to prevent accumulation of mucus, (*b*) to overcome constipation and intestinal toxemia, and (*c*) to improve general health.

(*a*) *To prevent accumulation of mucus* one of the best remedies is castor oil once or twice a week, and this may be supplemented by colonic lavage (colon irrigation) every day for a week, every two or three days for two or three weeks longer, or once a week for long periods of time. In colonic lavage, to enable the fluid to reach the cecum, the patient should be on the back, or perhaps for the first few minutes on the left side and then on the back, or rarely, in refractory cases, in the knee-elbow position. Preceding the lavage the bowels should be emptied, if necessary by an enema, in order to avoid starting up the defecation reflexes which will prevent the upward passage of the water, and to avoid carrying back feces from the rectum into the colon. The liquid used should be hot, and may be tap-water, normal saline, or sodium bicarbonate, 3j to Oj, of course sterilized (sodium bicarbonate is changed to carbonate by heat). The amount

required is usually 12 to 24 quarts, and it should be given slowly, with the reservoir about 2 feet above the patient. If the irrigation does not bring out the mucus, this may be expelled one to several hours later. I always consider that an irrigation is a failure if no water is retained to be evacuated later or if the water returns clear throughout, for obviously in such cases the liquid has failed to get past the descending colon or sigmoid.

To lessen the mucous production I have tried belladonna or atropin for many days at a time, but without avail. To promote its production, in the hope that this would prevent its desiccation and favor its expulsion, I have tried ipecac and emetin, also without avail.

(*b*) *The treatment of the constipation and intestinal toxemia* is by diet, laxatives, and mechanical measures. There should be insistence on a daily movement of the bowels, but restriction of the use of enemata and colon irrigations. I have had patients who came to think that any abnormal sensation could be removed only by enema or irrigation, and acquired the habit of using these several times a day. If there is ptosis of the abdominal viscera, laxity of the abdominopelvic walls (and these are exceedingly common), the patient should wear an inelastic binder for mechanical support, and should be put on exercises to help the abdominal muscles. I have called attention to these in articles entitled "Simple Measures in the Treatment of Chronic Intestinal Stasis" (International Journal of Surgery, April, 1914) and "The Medical Treatment of Chronic Intestinal Stasis" (Journal of the American Medical Association, August 29, 1914). In the latter I summarized the treatment as follows: "Regularity of defecation, measures to improve intra-abdominal pressure, measures to increase peristaltic activity, and measures to increase the bulk and softness of the colon contents. In the average case attention to habits of life and to the amount and kind of food, and the administration of a softening agent or a very mild laxative will be effective in overcoming the stasis, and, therefore, the toxemia. In severe cases the addition of an oil enema at night may work a marvellous change for the better. In these chronic cases the drastic cathartics should be omitted from use. If such measures

do not overcome the stasis and the toxemia, the question of surgery should be seriously considered."

Laxatives.—The best in these cases is usually a softening and bulk-producing agent, such as liquid petrolatum, milk of magnesia, cascara-agar (regulin), or phenolphthalein-agar, but these are not always either suitable or effective, and may need to be replaced or supplemented by phenolphthalein, cascara, senna, aloin, or rhubarb. These are tonic in type and may be used indefinitely. Cascara is prone to gripe because of the spastic tendency of the bowel. Salines may be employed for a short time, but not indefinitely, as they make an entirely abnormal stool. Drastics should be avoided. Calomel or blue pill is not contraindicated and may be useful as a weekly or occasional dose. I have already spoken of the use of castor oil weekly or semiweekly and the colon lavage. Hemorrhoids and anal fissure are bad complications, as they prevent the use of either castor oil or irrigations. They may be treated by the nightly instillation, with a soft-rubber ear syringe, of 60 c.c. (2 oz.) of warm olive or cottonseed oil.

A measure of great value in some persistent cases, especially if there is chronic colitis, is the retention of 4 to 16 ounces of olive, cottonseed, or mineral oil over night, every night for a month, a piece of rubber sheeting being placed on the bed and a folded napkin over the anus to avoid mishap. A capsule much in favor and apparently of value is that containing castor oil from 2½ to 10 minims with salol 2½ to 5 grains, given four times a day.

Diet.—This may have to be modified according to the condition of the stomach and upper bowel (achylia, hyperchlorhydria, gastric atony, etc.), but in general at the outset it should be of the bland lactofarinaceous type. Later there may be a gradual transition to a coarser type with much vegetable and fruit. But there should at all times be limitation in the amount of readily putrefactive proteins, as in animal flesh, eggs, beans, peas, and lentils, these being replaced, if possible, by much milk in the dietary. In some cases buttermilks are valuable, but not in the cases with hyperacidity or gastric atony. The coarse diet at the

outset, as advocated by von Noorden, is likely to give rise to gastric disturbances, particularly flatulence, and it is to be remembered that an excessive quantity of coarse indigestible food will do more damage to a sensitive intestine than any mild laxative. Moreover, in a large number of cases there is some real inflammation, and this is best treated by the bland diet. But the diet should be ample, and its quantity insisted upon, for these patients are prone to undereat because of a suspicion that this, that, or the other article of food does not agree with them.

Surgery.—If there is any definite surgical condition in the abdomen, such as appendicitis, cholelithiasis, adhesions, kinks or bands, these should be corrected. In 66 cases Mummery found surgical conditions as follows: in 14 adhesions causing kinks or obstructions, in 5 chronic appendicitis, in 2 inflammation of appendages or displacement of uterus, in 7 cancer, in 1 stricture of sigmoid. In persistent cases the bowel itself may have to be treated by surgical measures, viz.: (1) *To allow cleansing and medicating the colon*—as by appendicostomy or cecostomy for the purpose of permitting daily irrigations through the whole colon. These must be continued for from six months to two years (Mummery), and the procedure is not, in the author's opinion, a valuable one. (2) *To overcome stasis or to remove diseased portions of the bowel*, such as plication of the cecum, ileosigmoidostomy, cecosigmoidostomy, partial colectomy, and, very rarely, complete colectomy. The indications for radical surgery and the choice of surgical procedure I shall not attempt to discuss here.

(*c*) *Improvement in the general health may be obtained by*—

1. *Occupation, Recreation, and Rest in Proper Proportion.*—The patients should get up before breakfast and not lie in bed in the morning, should lie down when possible for one or two hours after the midday meal, and should retire early. They should not receive too many visitors or have pressure of social or business engagements, or unnecessary responsibilities added to the necessary ones. For example, a schoolteacher should not take extra college courses on Saturday and teach Sunday school on Sunday; a business man should not spend his evenings on club

committees or in study. Yet some recreation must be insisted upon, preferably attendance at games or playing games in the open air.

The great rule is that patients must *never get unduly fatigued;* yet I believe they are best off if they are not allowed to shirk all responsibility. Those with money tend to do so, and are prone to become chronic invalids, self-centered, hypochondriac, "hipped" on themselves, and leading useless lives. They go from one physician to another or to sanatoria, read numerous books about their disease and its treatment, and refuse to permit their ailment to be forgotten for a moment. These patients should be induced to avoid medical books and constant examination of their stools, and in every way should be encouraged to use their faculties and their muscles in a sensible manner, neither too much nor too little. A sensible nurse is a great help in managing the daily life of the female indolent patient.

2. *General hygienic measures*, such as cold spinal douches or alternating cold and hot douches, cold morning baths, cold rubbings up and down the spine, calisthenics, horseback-riding, golf, and general massage, with very gentle abdominal massage. A help in the treatment is a change of scene to get away from oversolicitious or nagging friends, or from the wear and tear of home or business. A visit to one of the spas may furnish rest and recreation amid pleasant surroundings, with hydrotherapy and the daily ingestion of laxative waters. It is well to remember that nervous people do not sleep or rest well in high mountainous regions.

3. *Stopping the use of tobacco and alcohol.*

4. *The administration of* (*a*) *iron* and *arsenic* as indicated by the state of the blood, (*b*) *bromids* for short periods in the highly nervous cases, (*c*) *strychnin* in cases in which the reflexes are not overactive, and (*d*) *alkalies* for acidosis or gastric hyperacidity.

Thyroid gland, atropin, emetin, and calcium I have tried without any good effect.

CONTRIBUTION BY DR. LEWIS GREGORY COLE

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ILEOCECAL INCOMPETENCY

Some of the Direct Causes; Constitutional Symptoms; Clinical Significance of the Incompetency.

IN my consideration of this subject I have been a coward, but I have paid the price, and herein, at the beginning of this paper, I wish to present the receipt in acknowledging the priority of Dr. James T. Case in publishing the findings of this condition. Dr. Case's roentgenologic observations on this subject have been extensively and accurately expressed in numerous communications, and the clinical and surgical aspects based largely on the roentgen diagnosis have been described in detail by Dr. Kellogg. I refer to this especially because some physicians, knowing personally of the work I did on this subject, at least two years before Case and Groedel's reports in 1912–13, have frequently referred to this work as antedating that of Case and Groedel.

This article, largely as it is presented tonight, was promised to Dr. Bassler in 1912 for the Journal of Gastro-Enterology, but I was pursuaded to let it season for a while before presenting it, and I now believe that it is sufficiently mellow and that the time is ripe for a presentation of this subject.

The term "ileocecal insufficiency," as used by the author on September 19, 1910, in reporting on the roentgenologic findings, is that condition of the ileocecal valve which allows the cecal contents to pass backward or regurgitate from the cecum into the ileum. I believe that the term "incompetency" instead of "insufficiency" of the valve is a much more satisfactory term.

Incompetency of the ileocecal valve can be detected in two ways, roentgenographically and surgically, and it may be suspected from the clinical symptoms of the patient. The roentgenographic way is a simple and accurate method of determining whether the cecal contents can pass into the ileum. Incompetency of the ileocecal valve can be detected surgically by milking the contents of the ileum away from the valve for a distance of 10

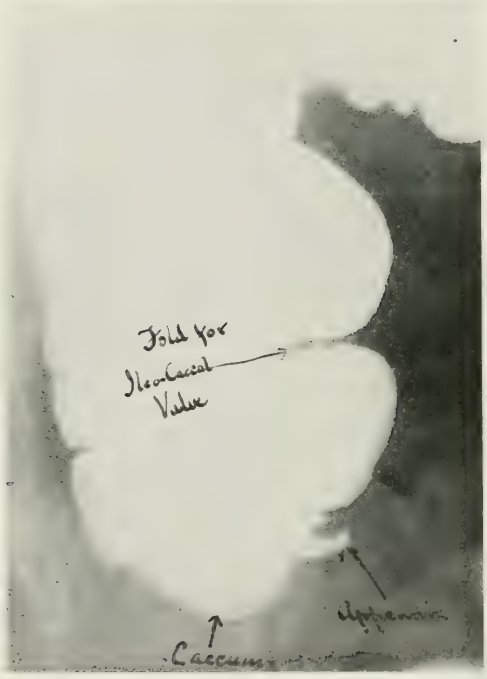


Fig. 49.—Normal cecum, except for appendix.

or 12 inches and noting whether or not the colonic contents are regurgitated into the ileum or whether the contents can be expelled into the ileum by manipulation of the colon. Postmortem tests of incompetency of the valve have been made by Birmingham, Charpy, Struthers, Cunningham, and others. Rutherford sums up these tests as follows: Want of uniformity in the description makes it probable that the ileocecal valve changes

soon after death, and concludes that the valve is normally competent during life. For further reference as to the anatomic construction of the valve I refer you to Rutherford's work. The antiperistalsis of the colon described by Cannon, which creates a back pressure against the ileocecal valve, shows the importance of the competency of the valve from a physiologic standpoint.

Fig. 50.—First degree of incompetency. Showing lips of valve.

In my original article I stated that some of the direct causes of incompetency were pregnancy and its sequelæ, chronic appendicitis with adhesions, postoperative adhesions, Lane's kinks, pericolonic veils, or Jackson's membrane. Any one of these conditions may be directly responsible for an incompetent valve.

The constitutional symptoms developed from the presence of an incompetent valve are due to the ileal absorption of putrid colonic contents, and a failure to repair the incompetent valve

ultimately forces the terminal ileum to assume a colonic function. The rich lymphatic supply of the ileum makes it ill suited for this function, as there will result an absorption of putrefying material.

At the time this paper was prepared observations had been made on approximately 1000 cases. The 300 cases out of the 1000 in which some degree of incompetency was shown by the

Fig. 51.—Second degree of incompetency, with marked deformity of cecum and valve.

influx of the cecal contents into the ileum are for the purpose of clinical study divided into three groups: First degree of incompetency, second degree of incompetency, and third degree of incompetency. These will be illustrated on lantern slides. Clinically, these three groups, depending largely on the amount of regurgitation, may be studied regarding the following considerations:

1. What factor other than the valve governs the amount of regurgitation?

2. Does incompetency of the valve allow habitual or periodic regurgitation?

3. Are the symptoms directly or indirectly caused by regurgitation?

4. What are the symptoms?

Fig. 52.—Third degree of incompetency, with extensive regurgitation all the way to the duodenum.

5. Can the symptoms be relieved by medication and diet?

6. Is surgical procedure ever indicated?

Each of these subjects have been fully considered in the complete article on this subject, but time does not permit me to discuss each of these in detail at this meeting.

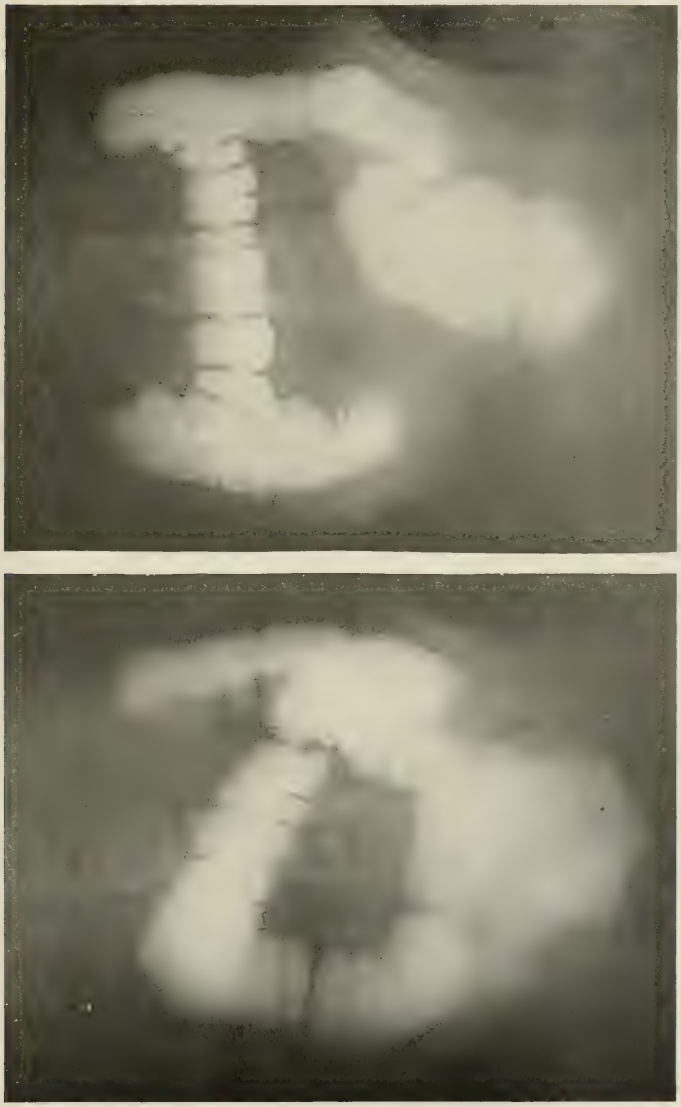
In considering the clinical significance of the incompetency I believe we must consider: 1. The amount of regurgitation that is

caused, viz., whether only a small amount of the colonic contents seeps through into the terminal ileum, or whether the valve is wide open and the colonic contents run all the way back into the duodenum. 2. Whether the clinical symptoms correspond with that group of symptoms which we recognize as occurring frequently in the second and third degrees of incompetencies.

Fig. 53.—Third degree of incompetency, with regurgitation of colonic contents all the way to the duodenum.

The symptoms directly at the valve are very slight unless the condition is associated with or caused by chronic appendicitis. Occasionally there is a case of very acute pain simulating gall-bladder or urinary colic and there is a distinct tumor mass in the right iliac fossa. I have seen only two or three patients with these attacks, but frequently one can obtain the clinical history of this condition from an intelligent observing patient, and in

my own mind I have associated this group of symptoms with the breaking open of the valve.

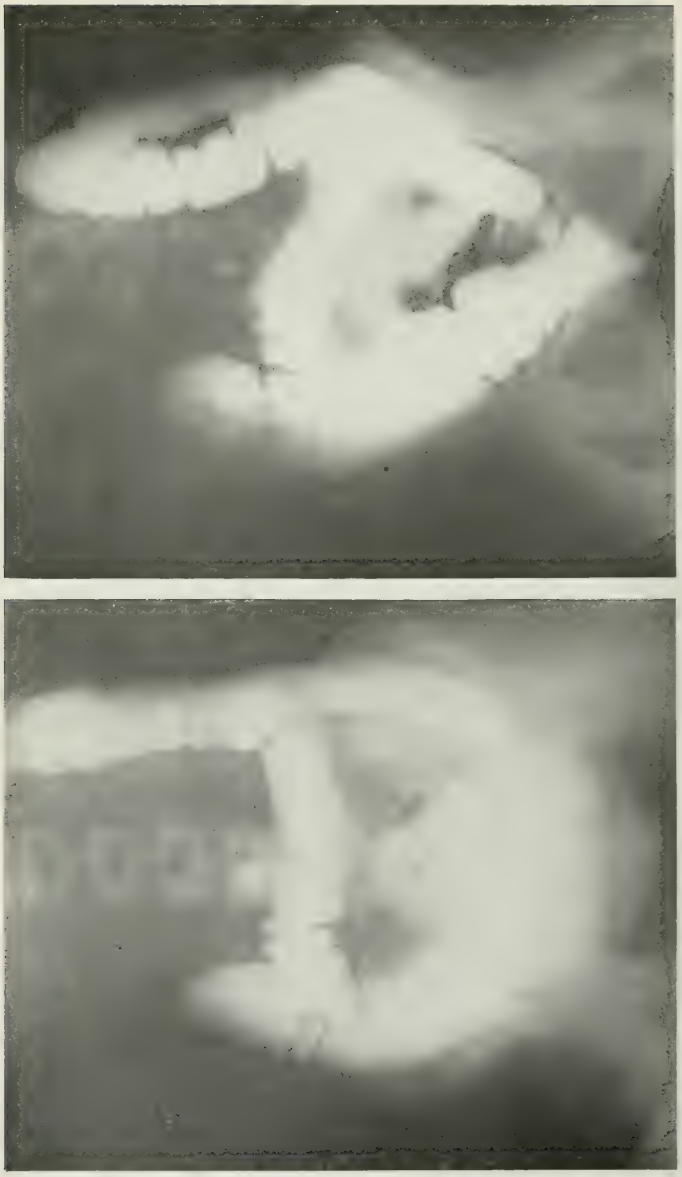


After Operation.

Before Operation.

Figs. 54 and 55.—Case 1: Referred by Dr. W. A. Bartlett. Operated on by Dr. J. P. Hoguet. Repair of valve held completely. Gastric ulcer excised. Symptoms competely relieved.

The constitutional symptoms are far more important, but they are so varied in the organ attacked that it is only by asso-



Before Operation. After Operation.

Figs. 56 and 57.—Case 2. Referred by Dr. W. F. Honan. Operated by Dr. W. F. Honan. Valve repaired and found competent year after operation. Symptoms ameliorated.

ciating them with the local symptoms, such as evidence of local pain to the left umbilicus accompanied by incarcerated gas and

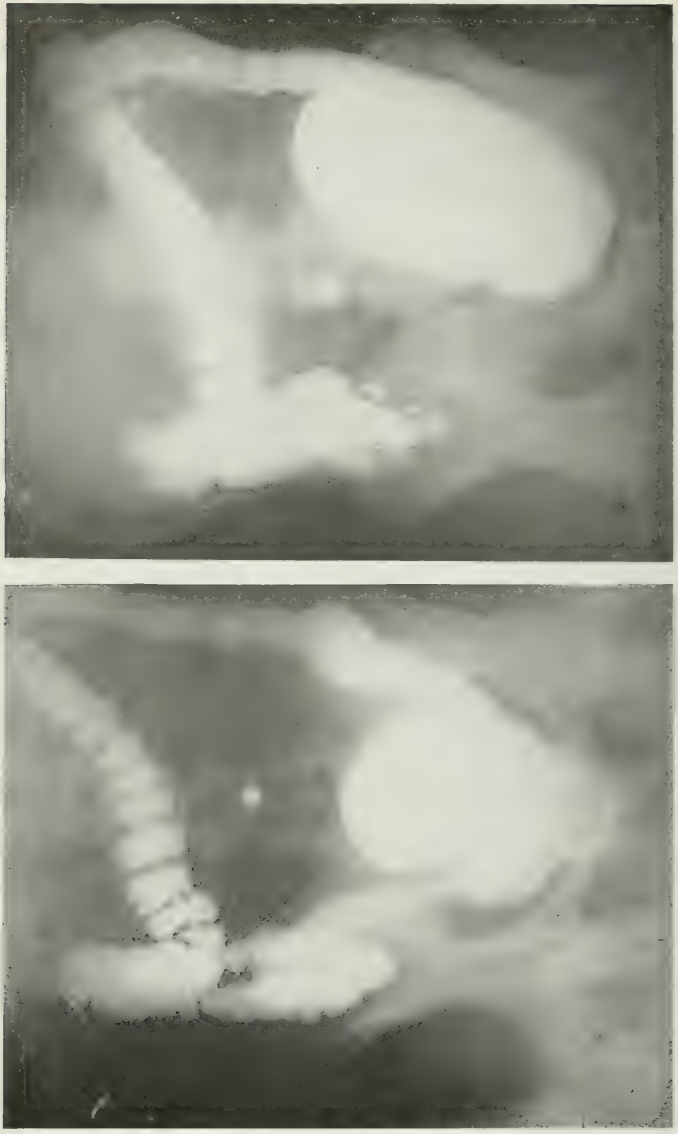
constipation, that one recognizes the approach of an attack. However, the periodicity is one of the most characteristic features

After Operation.

Before Operation.

Figs. 58 and 59.—Case 3: Referred by Dr. W. A. Bartlett. Repeatedly examined valve always found incompetent. Operated on by Dr. George E. Brewer. Repair complete. Symptoms completely relieved. Repaired valve held six months later.

of the constitutional symptoms. The classical symptoms of incompetency are periodic headaches, migraine, epilepsy, auto-



After Operation.

Before Operation.

Figs. 60 and 61.—Case 4: Referred by Dr. W. A. Bartlett. Operated by Dr. Chas. E. Peck. Repaired valve held six months later. Symptoms only partly relieved. Slight reflex gastric symptoms persisted.

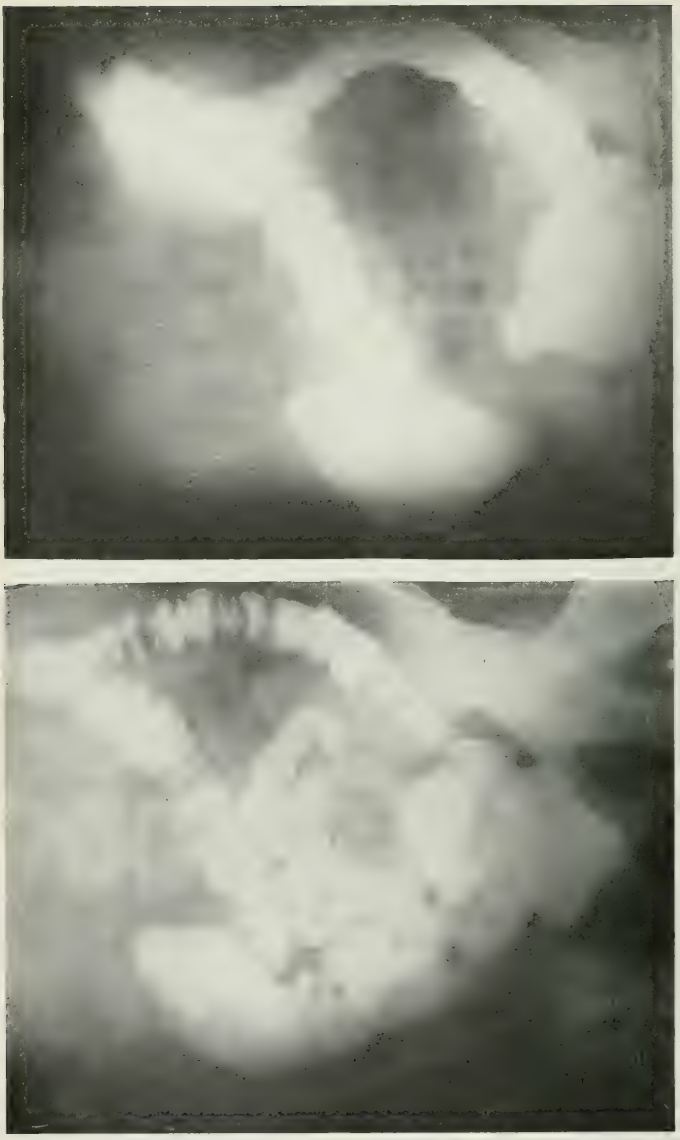
intoxication, and biliousness. It would be absurd, however, to state that all cases of headache, migraine, epilepsy, etc., were caused by ileocecal incompetency, but if these conditions are

After Operation.

Before Operation.

Figs. 62 and 63.—Case 5: Referred by Dr. W. A. Bartlett. Operated by Dr. G. E. Brewer. Repair of valve held completely eight months after operation. Symptoms completely relieved for year. Slight return of gastric symptoms, but only transitory.

associated with abdominal symptoms that are relieved, or if, as the patient says, they can be headed off after the bowels can



After Operation.

Before Operation.

Figs. 64 and 65.—Case 6: Referred by Dr. ———. Operated by Dr. Bodine. Symptoms absolutely relieved. Evidently better when I tried to have patient returned after operation. Last examination showed complete repair of valve.

be made to move freely, such cases should be examined for incompetency, and if it is found, they should be treated accordingly.

The relation between ileocecal incompetency and spasmodic or

organic lesions of the stomach is too extensive a subject to discuss in this paper and has already been discussed in another article. The close relationship between appendicitis and spasmodic or organic lesions of the stomach and duodenum is well recognized, and any physician knows that the first symptom of acute appendicitis is nausea or vomiting, and chronic lesions of the appendix or incompetency of the valve may likewise cause chronic spasm of the cap of the stomach.

The question of repair of the valve was not considered at the time this paper was originally prepared. I have advised surgical procedure for repair of the valve in the cases of which I shall show lantern slides. I have been present at the operations, and in many have taken active part in the operation, following as closely as possible the technic described by Kellogg, with care regarding certain details. The results have been most gratifying, and subsequent radiograms made after the repair of the valve have shown that in every case where the valve was properly repaired it has remained competent for a considerable period of time. Most of these repairs have been done too recently to determine whether or not the results are absolutely permanent, but my own conclusion is that if they are properly done they are permanent, and if they are not properly done they will not hold, and in many instances there is definite history of an acute attack, indicating the time when the valve broke open.

Space and time do not permit a complete clinical history of each case before and after the repair of the valve, but the roentgen examinations show that the valve may be repaired, and that in all but two cases that I have re-examined the repaired valve has been found competent.

Much more study on the relation of the clinical aspect of the subject compared with repeated subsequent roentgen examinations will be necessary before we can draw definite conclusions, but, considering how simple the operation is, and the relief that has been obtained in the few cases here reported, I am sanguine of the relief that may be given to some of these clinically obscure cases.

CLINIC OF DR. OSCAR M. SCHLOSS

BELLEVUE HOSPITAL

INTESTINAL INTOXICATION AND ACIDOSIS IN AN INFANT[1]

Presentation of the Case of a Baby aged Six Months. How to Diagnose this Condition. Etiologic Factor Uncertain; Either a Bacterial or Autogenous Chemical Poisoning. Diagnostic Factors, Especially Hyperpnea. Estimation of Blood Reaction; Sensitiveness of Respiratory Center to Same. Description of Tests for Acidosis. Misapprehension Regarding Urinary Acetone and Diacetic Acid. Conditions Bringing About Acidosis. Prognosis. Treatment. Postmortem Findings in Fatal Cases.

September 4, 1917.

THIS baby, a male, aged six months, was admitted to the Children's Service at Bellevue Hospital five days ago. The illness dated back three days, during which time he had eight loose green stools a day and vomited after each feeding. Before the onset of the illness his weight was 14 pounds; on admission he weighed 11½ pounds. Previous to the present illness he was fed a milk-and-barley-water mixture, on which he thrived until the diarrhea began. After the onset of the diarrhea he received barley-water only.

On admission the baby looked very ill. The eyes were sunken, the facial expression anxious. The respirations were from 36 to 44 per minute and were much deeper than normal. Inspiration was very deep and labored, indicating a mild degree of air-hunger. No cyanosis was present. The skin was dry and inelastic and

[1] From Dr. La Fetra's Service at Bellevue Hospital, New York City.

hung in folds, evidencing the great fluid loss. Rectal temperature was 99° F.

The behavior of the infant is worthy of mention. For a time he would lie quietly with eyes half-open and without expression. Suddenly he would become restless, moving his arms and legs violently and crying shrilly.

Physical examination showed nothing more of significance.

The laboratory data of importance was as follows: The corpuscular volume of the blood was 48 per cent., which was about 10 per cent. greater than the average normal. This indicated that the blood was more concentrated than normal, due to loss of water in the stools.

The blood count was as follows:

R. B. C.	6,100,000 per c.mm.
Hemoglobin	100 per cent. (Sahli).
W. B. C.	24,000 per c.mm.
Polynuclear cells	42 per cent.
Mononuclear cells	56.2 per cent.
Eosinophil cells	1.2 per cent.
Mast cells	0.05 per cent.

The carbon dioxid tension of the alveolar air was 18 mm.; the carbon dioxid combining power of the plasma of venous blood (Van Slyke) was 30 volumes per cent. at 0° and 760 mm. barometric pressure.

The urine was acid and the specific gravity was 1020. It contained a trace of albumin, a few granular casts, and a trace of sugar.

The patient was suffering from the form of toxemia frequently seen in cases of severe diarrhea. The toxemia is due either to poisonous products produced by bacterial growth in the intestinal tract, or to products elaborated in abnormal metabolism. Which factor is responsible we do not know. The appearance of these patients indicates definitely that they are suffering from some form of toxemia. The occurrence of this condition bears no absolute relation to the severity or duration of the diarrhea, although it is more likely to occur in the severer forms. There

are many cases of severe diarrhea, however, in which no toxic symptoms develop; on the other hand, severe toxic disturbances may occur in connection with but few watery stools or, rarely, with no diarrhea at all.

Since Howland and Marriott showed that many of these patients have acidosis, our conception of the disease has broadened considerably. In my citation of the patient's history you will recall that I emphasized the type of breathing. The rate was increased, but the striking feature was the increase in amplitude, especially of inspiration. In other words, the infant showed a mild grade of air-hunger such as one sees in diabetic coma. Breathing of this type is characterized as hyperpnea. This term was introduced by Haldane and simply means increased pulmonary ventilation. It is a better term than dyspnea, which is literally "painful breathing."

Hyperpnea is a very important symptom of acidosis, and, as a matter of fact, is the only clinical sign of value. The cause of the hyperpnea is the acidosis. We know that one of the most active and mobile mechanisms in the body is that which tends to keep the alkalinity of the blood at its normal value. As soon as the blood shows a marked increase in the amount of acid in proportion to alkali, in other words, an increase in the amount of acid, death occurs.

Our estimation of the blood reaction is usually in terms of hydrogen-ion concentration. As you know, all acids contain hydrogen, and the best and most accurate estimate of the reaction of an organic fluid is the concentration of the hydrogen ions. An increase in acidity or decrease in alkalinity is evidenced by an increased hydrogen-ion concentration. A decrease in acidity or increase in alkalinity is shown by a diminution in hydrogen-ion concentration.

Normally, the hydrogen-ion concentration of the blood is practically that of distilled water. While the hydrogen-ion concentration is the true criterion of acidity, we do not determine it as a diagnostic procedure for two reasons: (1) The method is complicated and requires special technic and apparatus; (2) through a mechanism, which I shall explain in a few moments,

the hydrogen-ion concentration is kept normal even though there is a considerable degree of acidosis.

As soon as fixed, non-volatile acids enter the blood-stream they neutralize part of the reserve alkali, and due to this cause the alkalinity of the blood would diminish and the hydrogen-ion concentration increase.

The respiratory center is very sensitive toward the least tendency of the blood to become acid, and with the slightest change in this direction the respirations increase in frequency and depth, which greatly augments the elimination of carbon dioxid. Carbon dioxid, as you know, is potentially an acid, H_2CO_3, and by its elimination from the blood the presence of foreign acids is compensated for and the hydrogen-ion concentration kept normal. In other words, carbonic acid is a volatile acid capable of excretion by the pulmonary epithelium, and when acids enter the blood which cannot be thus eliminated the ratio of alkali to acid is kept normal by the elimination of carbon dioxid. By this means the hydrogen-ion concentration is prevented from increasing.

The hyperpnea, therefore, represents the increased pulmonary ventilation, the object of which is to eliminate carbon dioxid from the blood.

I stated that hyperpnea is the only reliable clinical sign of acidosis. It is present in the majority of cases, but at times it is absent. For this reason in the cases without distinct air-hunger our diagnosis of acidosis must rest on laboratory evidence.

There are a number of tests which are more or less elaborate. I will not describe these, but will merely mention two of the simpler ones.

The first depends on the carbon dioxid content of the blood as measured by the alveolar air. During the passage of the blood through the lungs carbon dioxid is given off, so that the alveolar air has the same tension of carbon dioxid as the blood itself. By determining the carbon dioxid of alveolar air we can discover the amount of carbon dioxid in the blood. For the reasons given in the explanation of hyperpnea the blood carbon dioxid in acidosis is reduced. The simplest method for its determination

is the colorimetric method of Marriott, which was described in the Journal of the American Medical Association, May 20th, 1916. It can be carried out at the bedside and is very satisfactory, provided that the necessary precautions are observed. The normal tension of carbon dioxid in the alveolar air of infants is above 35 mm. In mild acidosis it ranges from 30 to 35 mm.; in moderate acidosis, from 25 to 30 mm. Below 25 mm. indicates a severe grade of acidosis.

The second method is the determination of the carbon dioxid combining power of the blood-plasma. This method was described by Van Slyke in the Journal of Biological Chemistry for June, 1917. It is a more accurate method than the analysis of the alveolar air, but has the disadvantage of requiring the withdrawal of blood. In very young infants, however, owing to the fact that their respirations are frequently shallow, the alveolar air analysis often gives results which are too low and may be misleading; in such cases the analysis of the blood-plasma is a great advantage. In normal infants the carbon dioxid combining power of the plasma of venous blood ranges from 53 to 70 volume per cent. at normal barometric pressure and 0° C. In acidosis the values are greatly reduced.

(Here one of the students made a suggestion.)

The suggestion that acidosis would be indicated by the presence of acetone and diacetic acid in the urine is often made. I am glad that this point was brought up, since there seems to be considerable misapprehension on this subject.

According to our present conception, acidosis means a diminution in the alkaline reserve of the blood. Nothing more, nothing less. Any condition, therefore, capable of bringing this about can cause acidosis. The possibilities are three in number:

I. Abnormal loss of alkali from the blood in ratio to the alkali absorbed from the food.

II. Through perverted or incomplete metabolism abnormal acids or abnormal quantities of normal acids are formed which neutralize the blood alkali. This is the form of acidosis which occurs in diabetes, in the so-called cyclic vomiting of children, and, at times, in ileocolitis. In these conditions the metabolism of

fat or of amino-acids from protein is incomplete and aceto-acetic acid and hydroxybutyric acids are unoxidized. These substances are capable of diminishing the alkali reserve of the blood.

III. We know that acids are normally formed in metabolism, and any condition which would prevent their excretion would cause a diminution of the alkaline reserve of the blood. Such a condition occurs in nephritis and also in the cases of acidosis due to acute diarrhea.

It is therefore apparent that the occurrence of acetone and diacetic acid bears relation to only one type of acidosis (Group II), and that these substances have no bearing on the type of acidosis under discussion, which belongs in Group III. It is quite true that we often find acetone and diacetic acid in the urine of these patients, but this is equally true of patients affected with measles, scarlet fever, and other diseases. Their presence is due merely to starvation. The true criterion of acetone body acidosis is the amount of these substances in the blood, and in the acidosis of diarrhea the amount in the blood is normal. The test for acetone bodies in the urine, therefore, is not a test for acidosis, and at most their presence may be due to a special variety of this condition.

As noted in the history, this baby showed a trace of sugar in the urine and the blood-sugar was also increased. The blood-sugar was 160 mg. per 100 c.c. of blood as compared with a normal maximum of 120. The hyperglycemia and glycosuria which frequently occur in this condition are probably due to the acidosis and not to any specific disturbance of sugar metabolism. It is not true, as many of the German writers assert, that the sugar in the urine is lactose due to the absorption of unchanged lactose through the injured intestinal mucosa. The proof of the fallacy of this idea is, first, that the sugar is frequently not lactose, but dextrose, and second, that many infants with intestinal intoxication have glycosuria and hyperglycemia when they are not receiving any milk or lactose in their food.

To return to the patient under discussion. As soon as the diagnosis of acidosis was made, he was given an intravenous injection of 100 c.c. of 4 per cent. sodium bicarbonate solution.

The injection was made into the superior longitudinal sinus, which, in our experience, is the most satisfactory vein to use for this purpose. If a scalp vein of sufficient size is present, it is perhaps preferable to select this, but unfortunately, in the patients with intestinal intoxication, the scalp veins are usually collapsed so that it is impossible to insert a needle. In entering the superior longitudinal sinus we use a No. 21 to No. 22 gage needle, $\frac{1}{2}$ inch long, and with a very short beveled point. With such a needle the danger of transfixing the sinus is very slight. The needle is attached to a syringe and inserted in the posterior angle of the fontanel and in a backward direction. While inserting the needle slight aspiration is made so that one can determine the moment the sinus is entered. We give the injections by gravity and never have the cylinder containing the solution more than 1 foot higher than the head of the patient.

The preparation of the bicarbonate solution is a matter requiring special attention. When a solution of sodium bicarbonate is heated to any considerable degree, especially when boiled, carbon dioxid is lost and sodium carbonate is formed. The change is indicated as follows:

$$2NaHCO_3 = Na_2CO_3 + CO_2 + H_2O.$$

Therefore if a solution of sodium bicarbonate is sterilized by boiling it is no longer sodium bicarbonate, but sodium carbonate. A concentrated solution of sodium carbonate injected quickly into the blood-stream might prove toxic, but if the solution is allowed to flow slowly into a vein it is perfectly safe, for there is sufficient carbon dioxid in the blood to change the carbonate into bicarbonate as soon as it enters the blood-stream. The reverse of the chemical action given takes place. This is true unless the carbon dioxid of the blood is extremely low. As a rule, we do not hesitate to give sodium carbonate intravenously if the CO_2 tension of the blood is above 20. When the tension is below 20 (extreme acidosis) it is well to prepare the alkali in a special way so that there is no sodium carbonate present. For subcutaneous injections the use of sodium bicarbonate is imperative, for an

appreciable amount of sodium carbonate injected into the subcutaneous tissues would cause severe necrosis or gangrene of the skin.

To prepare a sterile solution of sodium bicarbonate one of two methods may be followed. The ideal method is to make up the solution of desired strength and to sterilize it in an autoclave or by boiling. A few drops of a 1 per cent. alcoholic solution of phenolphthalein is added, which turns pink owing to the presence of the sodium carbonate. Carbon dioxid from a cylinder or generator is then passed through the solution until the pink color disappears. When this occurs the carbonate has been changed to bicarbonate and the solution is ready for administration. This method was suggested by Magnus Levy.

The second method consists in using a sterile preparation of sodium bicarbonate. There are several brands of sodium bicarbonate which rarely contain micro-organisms. Needless to say each lot should be cultured. The water is boiled and then cooled, and the sodium carbonate dissolved in the cooled solution, which is then slightly warmed before injecton. All the water should be freshly distilled. For intravenous injection a 3 to 5 per cent. solution is used. For subcutaneous injection a 2 to $2\frac{1}{2}$ per cent. solution is administered.

The actual amount of sodium bicarbonate to be given depends somewhat on the age and weight of the patient and also on the degree of acidosis. It is impossible to obtain an exact formula based on these factors by which the dose can be gaged. As a rule, from 2 to 6 grams of bicarbonate must be given to bring the blood bicarbonate to normal. The blood or the alveolar air, preferably both, should be tested every eight to twenty-four hours after the bicarbonate has been given to serve as a guide for further treatment. As a rule, if the grade of acidosis is severe, it is wise to give from $\frac{1}{2}$ to 1 ounce of a 3 per cent. bicarbonate solution by mouth every three hours as long as the diarrhea lasts or until there seems to be no possibility of a recurrence of the acidosis.

(A student here asked why the alkali is not given by mouth instead of by intravenous or subcutaneous injection.)

It is our experience that sufficient bicarbonate cannot be given in this way to correct a severe acidosis as quickly as should be done with these very sick patients. Perhaps on account of the diarrhea much of the bicarbonate is not absorbed, and in many instances these infants will not take or retain a large amount of the drug. According to our observations the milder grades of acidosis alone can be corrected by giving bicarbonate by mouth exclusively.

As stated previously, this baby was given 4 grams of sodium bicarbonate intravenously. The next day the alveolar air had a CO_2 tension of 40 mm. and the CO_2 combining power of the blood-plasma was 80 volumes per cent. The latter value is equivalent to a CO_2 tension of 52.8 mm., which is considerably higher than the alveolar air. This is usually the case after a sufficient dose of sodium bicarbonate has been given into a vein. A more striking evidence of the correction of the acidosis was the appearance of the infant. Within an hour the face lost its drawn appearance and the infant was breathing quietly without evidence of air-hunger. He also became alert and more comfortable.

The acidosis disappeared after the single injection of alkali, and at present (five days after treatment) the blood bicarbonate is still normal. Today the CO_2 tension of the alveolar air was 39 mm. and the CO_2 combining power of the plasma of venous blood was 60 volumes per cent., which is equivalent to a CO_2 tension of 39.6 mm.

The baby was fed only a thick barley gruel with $\frac{1}{2}$ ounce of protein-free milk in a 30-ounce mixture for two days, and then was given 6 ounces of boiled skimmed milk diluted with the above mixture; six feedings of 5 ounces in twenty-four hours. The milk has been increased so that he is now receiving 10 ounces of milk in twenty-four hours.

His weight is now $12\frac{1}{4}$ pounds, as compared with $11\frac{1}{2}$ pounds on admission. The increase of weight merely indicates that the water has been retained, for the food has obviously been too weak to permit a retention of fat or nitrogen. It is well to bear in mind that the water metabolism in infants is extremely active,

and most sudden losses or gains in weight are due in great part to a loss or gain in water.

The all-important question must now be confronted. Will the infant recover? The answer depends entirely on his ability to digest and assimilate food. We frequently see patients of this type improve to the same degree that this one has improved, and then die, owing to the fact that there is a recurrence of the intoxication, or that the patient cannot assimilate sufficient food for his nutritive needs. In the latter event, death is due to malnutrition. Despite the improvement which occurs when the acidosis is corrected, a large percentage of the infants with intestinal intoxication die. The acidosis is only a symptom due to some intestinal infection or to some underlying nutritional fault. While the correction of the acidosis is important and unquestionably gives an opportunity for recovery, yet a further reduction in the mortality of intestinal intoxication must await more adequate knowledge of the actual etiology which is now unknown.

Postmortem examination of patients who die from intestinal intoxication reveals little that is significant. The intestinal mucosa is rarely congested, but, as a rule, is pale and somewhat atrophic. Small erosions of the duodenal mucosa occur in some cases, but are of no definite significance. The liver is often fatty and shows some degree of parenchymatous degeneration. Very frequently the kidneys are pale and swollen and show distinct evidence of parenchymatous nephritis. The lack of significant anatomic changes in this disease seems to indicate that the etiology lies in some chemical poison elaborated in the intestinal tract or produced by perverted metabolism.

CLINIC OF DR. ALFRED F. HESS

Home for Hebrew Infants

VAGINITIS (CERVICITIS) IN INFANTS

The Cause of the Infection; Pathology; Diagnosis; Symptoms; Complications; Prognosis; Treatment.

One of the most difficult problems that physicians who are caring for infants have to contend with is that of vaginitis. Though this is a familiar story to the children's specialist, it is probable that those who do not specialize in the diseases of children, and who in the course of their practice do not see a large number of infants, hardly realize the extent of this infection.

There is a prevailing impression not only among the laity, but among the medical profession at large, that vaginitis is more particularly a disease of institutions; that it is rarely found in the home, and is practically confined to the infant and foundling asylums. Such, however, is by no means the case. It is, naturally, impossible to give exact figures and data as to the prevalence of an infection of this kind in the home, but my experience has been that in New York City almost 50 per cent. of the female infants of the poor are affected by this disease. These figures may be somewhat too high; they are, however, based upon the records of infants for whom admission is sought at the Home for Hebrew Infants in this city. For some years we have been compelled to reject about 50 per cent. of these female infants on account of vaginitis. They do not come to us from other institutions, but from the homes of the poor. The result of having to refuse admission to so many girls is that at all times our census

shows about two-thirds male children to one-third female. It is very apparent, therefore, that this is a subject which should be thoroughly understood and appreciated.

The cause of this infection is the gonococcus, the same micro-organism which leads to urethritis, vaginitis, and the many associated inflammations in adults. Occasionally it may be due to some other micro-organism; for example, recently I had a case which was due to the streptococcus. From a broad clinical point of view, however, it is safe to consider vaginitis as due to the gonococcus and synonymous with gonorrheal vaginitis.

It is difficult to state exactly how this infection takes place, whether it comes about through infected diapers, or whether it is transmitted directly by hands carrying the infectious micrococcus; but it is clearly a contact infection. In some institutions which have been plagued with this persistent disease, diapers are used but once and destroyed after using. In the home there is no doubt that the baby is often infected by the father, mother, or some other adult in the household suffering from gonorrhea. I have known of one instance in an institution where a small epidemic was brought about through an infected nurse. In institutions, however, the main source of infection is the baby who is harboring the gonococcus. Infants are so susceptible to this form of infection that if a case gains admission to the children's ward we can be sure that other cases will develop in the near future.

This marked susceptibility wears off spontaneously in early childhood, so that we find children two or three years of age far less subject to the disease than younger infants. Furthermore, there is an individual difference as regards susceptibility. Once in a while we meet with a baby who is able to live in an infected environment, and, in spite of long exposure, remain free from infection.

The great source of danger in institutions is the gonococcus carrier. A baby is admitted to the ward apparently free from infection; not only does it manifest no trace of vaginal discharge, but microscopic examination shows an entire absence of gonococci. As a result, however, of some intercurrent infection accompanied

by fever, an old, quiescent vaginal inflammation is rekindled, a vaginal discharge containing gonococci is incited, and before we are aware of the danger, infection has spread to other infants. It is the same danger as exists with diphtheria and typhoid fever—*the danger of the latent carrier.*

Pathology.—Naturally, very little opportunity is afforded to study this infection from a pathologic point of view. In the first place, very few institutions admit these cases, and, furthermore, the disease is a mild one not resulting in death, so that postmortem examination is rare. It is only possible where an infant happens to have a vaginitis as a secondary complication to some fatal disease. At our institution I have had five opportunities to study the uterus, vagina, and adnexa in these cases. Macroscopically, there is surprisingly little to be seen: the external os of the cervix is slightly reddened, the wall of the vagina may show slight excoriation, but the body of the uterus and its appendages in all the cases were found to be normal. Microscopic examination likewise reveals but few changes. In many instances the vagina is normal, and all that is to be seen is some submucous infiltration of round cells at the external os of the cervix.

It is for these reasons that, from a pathologic viewpoint, it is more exact to term this infection "cervicitis" than "vaginitis." It is probably due to the fact that the gonococci find a favorable habitat in the glands of the cervix that it is so exceedingly difficult to cure these cases and eradicate the micro-organisms.

Diagnosis.—The diagnosis of vaginitis, or cervicitis, is very easy in the outspoken cases, but exceedingly difficult where the infection is mild or non-active. In the typical cases, with a marked, profuse, yellow, excoriating discharge, it needs but a glance to make the diagnosis. In other instances, where the discharge is but slight, where there is but a faint stain on the diaper, a microscopic examination is necessary in order to be sure of one's ground.

The method of making the microscopic examination is very simple, but very important. It is not sufficient merely to take a smear from the labia, as is usually done, but we must obtain

material from the depth of the vagina, from the tip of the cervix itself. To this end, a probe covered with cotton and moistened in water is inserted far into the vaginal canal until it meets the cervix. It is then withdrawn and a spread is made on a slide or cover-glass for microscopic examination after staining with the Gram stain. Even then the diagnosis is often difficult unless intracellular diplococci are found. If only a few pus cells are seen, it may be impossible to state absolutely whether we are dealing with a true case of vaginitis; it is well, however, to consider all cases highly suspicious which show pus cells on such examination. It has been the general experience that in almost every instance such infants, at some former time, have had an active vaginitis.

For the past few years we have made use of vaccines in order temporarily to excite a latent inflammation, and in this way enable a diagnosis. To this end, gonococcus vaccine has been injected subcutaneously in 250,000,000, 500,000,000, and 750,000,000 doses, with three-day intervals. During the past year, as a result of such *provocative injections*, we have discovered 8 cases during the first week or two following admission. We have made use of this method also in wards where vaginitis has arisen, in order to uncover and discover latent cases. These provocative injections are not to be considered specific treatment, as injections of staphylococcus vaccine seem to bring about very much the same result.

For a considerable period we tried the use of complement fixation in order to determine whether in this way we could be apprised of the early infections. It was not, however, found to be useful, and we no longer employ it for this purpose.

Symptoms.—As I said before, almost all the female infants are highly susceptible to vaginitis, some being more so than others. The male infant rarely develops a genito-urinary infection, as he is protected by the small opening of the urethra. The cases which I have seen have been regarded as the result of gross carelessness; they ran a very favorable course, the infection passing away in the course of ten days or two weeks and causing no disturbance whatsoever. In view of the fact that they were so

mild, as well as that they showed a negative complement fixation reaction, it is probable that only the anterior urethra was involved.

The typical case of vaginitis is usually a fairly well-nourished baby, not to be distinguished in general condition from one free from the infection. The disease causes the infant little disturbance. There is merely a more or less marked vaginal discharge with some irritation of the vulva, and occasionally the child is somewhat fretful or evinces signs of pain on urination.

Complications.—The complications are what render the disease one to be feared and guarded against. Although they occur infrequently, they are most serious. The main one is gonorrheal ophthalmia. This is a danger for the child itself and for the adults who surround it; it is one which should be constantly borne in mind, one which every children's specialist and many other physicians have encountered from this source.

Gonorrheal arthritis is also met with. This inflammation occurs, in my experience with exceptional frequency, in children who have a chronic vaginitis and develop scarlet fever. This has been our observation at the Willard Parker Hospital for Contagious Diseases in New York City.

The severest complications are those due to an ascending infection into the body of the uterus and the tubes. We may have a salpingitis, with symptoms resembling an appendicitis. Indeed, this possibility must always be considered and investigated before diagnosing appendicitis in female children. A still more severe complication is gonorrheal peritonitis; the literature contains many such cases with fatal outcome.

Prognosis.—This is good as to well being; as to cure it is quite otherwise. Few infections persist so stubbornly and show such marked chronicity. There is a decided difference of opinion as to the period of time which the average case lasts. Some observers believe that the condition exists throughout childhood and into womanhood. All agree that it may last for years. I have seen cases which have persisted three and four years, but I have also seen others which were cured in six to eight weeks, as verified by a subsequent observation of years. It is, indeed, contended that this vaginitis is a frequent cause of sterility among

women, but there is nothing in the pathology or course of the disease that allows us to make this deduction; indeed, all facts point to the improbability of such an event except as a rare occurrence.

Treatment.—From the point of view of prophylaxis, it should be the rule that if any member of a household has a gonorrheal infection, he or she should not handle a female infant. If this is not practicable, then all precautions should be observed to avoid communicating the infection. The mother should be warned of the danger, and urged to wash her hands thoroughly before diapering or bathing the baby. One thing which leads to frequent infection is the unnecessary toilet of the vulva in infants; the less these parts are handled, the fewer will be the number of cases of vaginitis.

As regards active treatment, the number of drugs which have been recommended is legion. They include almost all the antiseptics, such as nitrate of silver, boric acid, potassium permanganate, weak solutions of corrosive sublimate, not to mention the various newer antiseptics. None of these, however, has been found to have a decided superiority; the one gives quite as good results as the other. The best treatment is to use an antiseptic solution, for example, bichlorid of mercury, 1 : 5000, employed as a daily douche; the main requisite is that a sufficient amount of the solution be used. A douche bag should be filled with 2 quarts of the solution and a thorough irrigation of the vagina and cervix be carried out. In this way the parts will be kept clean and further inflammation be prevented.

Some years ago we attempted the topical application of antiseptics to the cervix, a speculum being introduced into the vagina and a strong solution of nitrate of silver or other antiseptic applied frequently. Our results, however, were not such as to warrant recommending this form of treatment, which is quite difficult to carry out. We also made use of irrigations of yeast, which has been recommenced and used considerably in adults, but which did not seem superior to irrigation with antiseptic solution.

For the period of a year our cases were treated with gono-

coccus vaccines. They received large doses two and three times a week. The treatment was carried out faithfully, but the cases cannot be said to have shown any marked improvement over those otherwise treated. The keynote, therefore, of active treatment is cleanliness. A pad of gauze should be placed over the vulva and renewed often in order to save the diaper from marked contamination. The diapers should be kept in antiseptic solution until they are washed, and should be subjected either to live steam or to boiling water. All the utensils (especially the thermometer) which are used for the child should be kept separate, and by no means be employed in any way for the use of any other female infant. If these simple measures are carried out the cases will get well. Whether they last weeks or months depends to a large extent on the individual susceptibility of the infant.

CLINIC OF DR. ROBERT ANDERSON COOKE

POST-GRADUATE HOSPITAL

PROTEIN SENSITIZATION IN THE HUMAN WITH SPECIAL REFERENCE TO BRONCHIAL ASTHMA AND HAY-FEVER[1]

Generalization on the Subject of Protein Sensitization, Experimentally and in the Human: Active Sensitization, Passive Sensitization. Pathogenesis. Multiple Sensitization. Diagnosis; Description of Methods. Bronchial Asthma; Specific and Non-specific Causes. Demonstration of Case. Therapy. Prognosis.

Hay-fever, or Pollinosis. Causative Agent. Two Divisions, Early and Late Types. Demonstration of Case; Early Hay-fever; Test for Pollen Reactions; Therapeutic Dosage Outlined in Tables. Demonstration of Case of Late Hay-fever; Test for Pollen Reactions; Therapeutic Dosage Outlined. Prophylaxis. Prognosis. Warning Against Carelessness. Brief Résumé of Other Conditions of Sensitization.

June 4th, 1917.

IN endeavoring to cover all the points of the subject of my lecture this morning, and that of tomorrow morning, it will be necessary to deal very briefly with some of them. I have decided to speak rather generally of the subject of protein sensitization in the human this morning, and to take up a little later that of bronchial asthma, leaving hay-fever until tomorrow, to be followed by a brief discussion of a few of the other clinical types.

Active Sensitization.—If we inject an animal with a small amount of some form of protein, the body cells of this animal begin at once to produce immune bodies that are specific against that form of protein. The production of these antibodies begins

[1] Two lectures delivered June 4th and 5th at the Clinics of the American Medical Association Annual Meeting in the Post-Graduate Medical School and Hospital.

at once. At the end of a certain time—which is the incubation time—these antibodies have been produced in such quantities that on reintroduction of a minute amount of the same type of foreign protein as was originally introduced, certain clinical symptoms, oftentimes producing death, result. These symptoms represent what is generally termed "anaphylactic shock."

I can best illustrate this by supposing a few typical experiments:

I. If we inject a guinea-pig intravenously with 1 c.c. horse-serum, no symptoms whatever occur. This shows that the horse-serum itself is not toxic.

II. Let us inject a guinea-pig with 0.01 c.c. horse-serum and the next day inject 1.0 c.c. horse-serum and no symptoms follow.

III. We inject a guinea-pig with 0.01 c.c. horse-serum and allow an interval of ten to fourteen days to elapse, the introduction then of 1 c.c. of horse-serum is followed immediately by symptoms of anaphylactic shock, with death. Here the animal has become sensitized in the ten- to fourteen-day interval, representing the incubation period, during which time the antibodies were being formed. In the first two experiments they had not yet been formed in sufficient quantity to produce symptoms.

IV. Suppose we inject a guinea-pig with 0.01 c.c. horse-serum, allow an interval of ten months to elapse, and then introduce 1 c.c. horse-serum; immediately the symptoms of anaphylactic shock with death ensue. In other words, an animal once actively sensitized remains so.

V. If we inject a guinea-pig with 0.01 c.c. horse-serum every day for ten consecutive days and on the eleventh day inject 1 c.c. horse-serum, no symptoms result. This animal has become immunized.

VI. If we allow such an animal to wait an indefinite period, six months to a year, and then inject 1 c.c. horse-serum, the symptoms of anaphylactic shock and death follow. This shows that the animal, previously immunized, has returned to the sensitized state.

VII. If we inject an animal with .01 c.c. horse-serum and allow the incubation period to elapse and then inject a sublethal

dose of the foreign protein—that is, a dose that will produce symptoms but will not produce death—we can immediately thereafter inject as much of the foreign protein as we desire without producing any symptoms whatever. This shows that the sublethal dose has united with the antibodies, that they are for the time being thrown out of commission, so to speak, and the further introduction of the protein is as ineffective as though the animal had never been treated. This is what is known as anti-anaphylaxis or desensitization.

The explanation for all this is as follows: The introduction of foreign protein into the tissues of an animal stimulates certain cells to produce immune bodies which are specific for the protein introduced. It takes time to produce these immune bodies as shown by a comparison of experiments II and III. This is the incubation period and is analogous to the incubation period of all infectious diseases. These immune bodies tend to attach themselves to certain cells. When a single, small dose of antigen (protein) is introduced, the number of antibodies is small and all tend to attach to cells. If a large or repeated injection of antigen (protein) is given, the antibodies are correspondingly increased, and, while part is attached to cells, the remainder circulates freely in the blood. It is the union of antigen to the attached cellular antibodies that produces the symptoms. Where antibodies are small in amount and attached, the introduction of antigen produces symptoms at once. When the antibodies are in excess and circulating free as well as attached, the injection of antigen does not produce symptoms, as the free antibodies have united with the antigen and protect those attached.

To sum up: When antibodies are few and attached, we have the sensitized or anaphylactic state. When they are in excess, we have the immune state. In other words, anaphylaxis and immunity are in principle the same; they differ only quantitatively.

In the guinea-pig, on which these experiments are most readily performed, it has been determined that death results from asphyxia, the result of the contraction of the smooth muscles in the bronchi.

Passive Sensitization.—If we take serum from an animal that has been actively sensitized and introduce it into a normal animal and allow a period of time to elapse—usually forty-eight hours—the second animal can be shown to be sensitized to the same protein that was originally used to sensitize the first animal. The introduction of the original foreign protein into this second animal produces symptoms of anaphylactic shock in the same way that it did in the first. In other words, there has been a transfer of immune bodies from the first animal to the second by means of the serum, thus passively sensitizing it.

Application To The Human.—All this experimental work, while not in itself as yet complete, has given us sufficient data for the application of these same principles to the human body. It is possible to actively sensitize human beings to foreign protein in exactly the same way that the guinea-pig can be sensitized. There is, however, this apparent and important difference, that a human being actively sensitized in this artificial way to a foreign protein does not, of necessity, remain permanently sensitized.

There are, on the other hand, a number of clinical conditions which have been put in the anaphylactic group, in which the sensitization has occurred not through any known artificial channel, but in an unknown natural way. It is with these natural sensitizations as they occur in the human body that we are most concerned, and it is in this group that we find such clinical manifestations of sensitization as bronchial asthma, hay-fever, angioneurotic edema, acute gastro-enteritis, and a few other less definitely decided conditions, such as certain chronic arthropathies, renal disease, and epilepsy.

You will remember that, speaking in general at the beginning of this discussion, I made the remark that the antibodies tend to attach themselves to the cells of certain tissues. When it happens that the cells which are sensitized are the smooth muscle-fiber cells of the bronchi, and the mucous membrane throughout the bronchial tract, the anaphylactic symptom induced is bronchial asthma, the narrowing of the lumen of the

bronchioles being due both to constriction of the circular muscle-fibers and edema of the mucous membrane.

When the sensitized cells are those of the mucous membrane of the eye, nose, and throat, the symptoms when produced are those typical of hay-fever. In the same way, it is the cells of the skin that are sensitized in urticaria; the connective-tissue cells that are sensitized in angioneurotic edema, the cells of the mucous membrane and smooth muscle-fibers of the intestinal tract in gastro-enteritis, and so on.

Pathogenesis.—So little is definitely known with regard to the pathogenesis that I will only mention the fact that we have been able to show in the study of a large series of sensitized cases that the sensitization is an inherited characteristic, that it appears to be *dominant* in the Mendelian sense of the word, that the inheritance is not one of sensitization, but rather one of the capacity to become sensitized. The study of our cases has shown that the sensitization is just as frequently different as it is similar in forebear and descendant.

Multiple Sensitization.—It is also important to realize the fact that humans who have this tendency to become sensitized do not limit themselves to a sensitization to some one protein, but are frequently sensitized to several. In fact, over 50 per cent. of the people that are sensitized at all show multiple sensitization.

Diagnosis of Sensitization in Humans.—There are two methods by which sensitization can be detected:

(1) The cutaneous reaction. Fortunately, in the interests of diagnosis, the cutaneous cells are frequently sensitized even though they are not involved directly in the clinical type of the disease. For instance, in hay-fever the symptoms limit themselves to the mucous membrane of the eyes and the upper respiratory tract; urticaria is not present, although the cells of the skin are sensitized exactly as are the mucous membranes. The absence of urticaria in hay-fever is due to the fact that the protein itself is not absorbed into the blood-stream in sufficient quantity to produce a generalized reaction.

These skin tests may be made in a number of ways. The

protein with which we are testing may be rubbed in through the unbroken skin. This is not satisfactory on account of the fact that there are many patients with an irritable skin in which an urticarial wheal or tache cérébrale occurs on slight provocation.

Another method is that of scratching through the superficial layer and with gentle friction rubbing the protein in.

Personally, I prefer the intradermal test in which a minute amount of solution of the protein is injected into the superficial epithelial layers. This is done with so much less trauma and brings the protein into such intimate contact with the cells that the reactions are much more satisfactory. I will show you on the case that we are to study this morning exactly what I mean by positive reaction. You will notice a definite wheal, often with pseudopod-like projections and a surrounding zone of hyperemia (Plate 1, Fig. 2).

(2) Ophthalmic reaction. In a number of cases the mucous membrane of the eye is also sensitized and the instillation of a minute amount of protein solution, or even a powder, produces almost at once corneal and conjunctival injection and edema with intense lacrimation and itching of the eye. This reaction, too, I will be able to demonstrate this morning (Plate 1, Fig. 1).

BRONCHIAL ASTHMA

The type of protein sensitization that I wish to take up particularly with you this morning is bronchial asthma.

That bronchial asthma is an anaphylactic manifestation was first suggested by Meltzer, the analogy between artificial anaphylactic shock in the guinea-pig and bronchial asthma in the human being so striking that the theory was inevitable and was very shortly proved to be true. Take, for example, that very common type of bronchial asthma that results from exposure to horses; the injection of horse-serum, usually given in the form of an antitoxin, has produced in many well-authenticated cases immediate death, simulating in every way the anaphylactic shock of experimental animals.

On the other hand, there are certain cases of bronchial asthma that we are not as yet able to put into the anaphylactic group.

PLATE I

Fig. 1.—Showing moderately positive ophthalmic reaction following instillation of pollen solution.

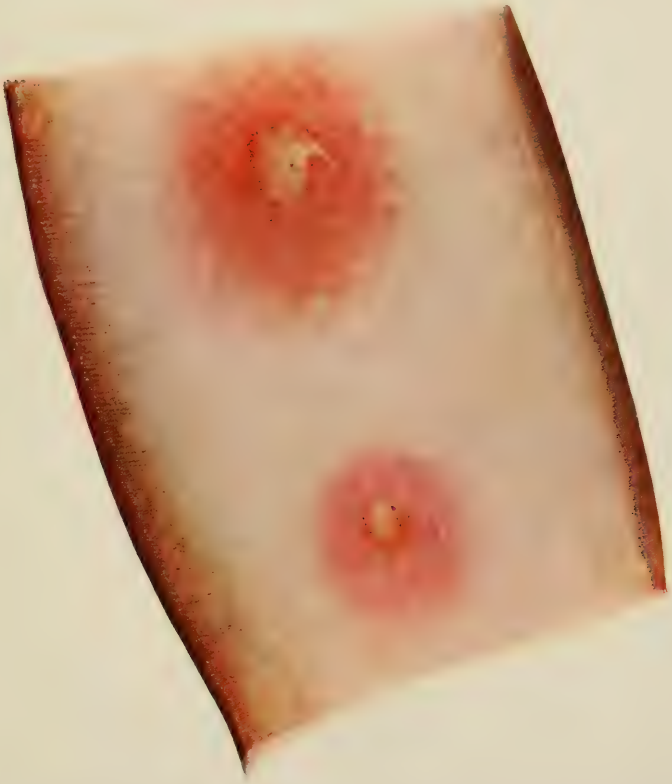


Fig. 2.—Showing two reactions, the upper one marked, the lower one slight, following intradermal injections of pollen solution.

It is wise, therefore, to classify our cases of bronchial asthma as follows:

I. Specific, or anaphylactic causes. Foreign protein absorbed from—
   1. Respiratory tract:
      (*a*) Animal emanations.
      (*b*) Vegetable emanations (pollen).
   2. Alimentary tract food proteins.
   3. Foci of chronic infection—bacterial proteins.
   4. Subcutaneous or intravenous injections.

II. Non-specific, or not demonstrably anaphylactic.

Non-specific Causes.—It is well known that specific causes do not cover the entire field. Many cases of asthma give a definite and distinct history of the development of an attack from exposure to intense cold, violent exercise, especially after a hearty meal and the inhalation of irritating dust and vapors. All such cases can be grouped under the general heading of non-specific origin, for in a careful study of each case of bronchial asthma it is usually easy to discover that these factors are not operative until the condition has become established and the so-called *asthmatic habit* has been developed. On the question of this *asthmatic habit* we will have something to say later on this morning.

With this as a basis for our study, I want to present the following case of bronchial asthma, and we will go through the routine of an examination in order to give you a concise idea of how the cases are approached for individual consideration.

The history, briefly, is as follows: The man is thirty-six years of age and gives a negative family history. He had pleuropneumonia four years ago, and this accentuated the asthmatic tendency which had existed previously for years. He has had three operations on his nose, during which the turbinates have been removed and the septum straightened. He had hives once or twice as a boy. Habits are good and sleep is fair except when disturbed by the asthma. He has lost much weight in the last two years; in 1914 he weighed 156 pounds and at present his weight is only 133 pounds.

Present History.—Has had asthma since he was four years of age. It was severe until he was eight years of age. The attacks were brought on by exposure to horses; he suffered also in the winter time, when they were occasioned by bronchitis. After he was ten years of age he suffered little until his attack of pleuropneumonia four years ago, since which time he has been completely disabled. During these four years his asthma has been more or less continuous, with periodic exacerbations. At times the attacks have been so severe that he has required morphin to control them, but occasionally the ordinary asthmatic powders give relief. At times the cough is severe and there is a large amount of thick, mucopurulent expectoration. He has a tendency to constipation and is bothered more or less all the time by gastric indigestion with symptoms of flatulence, pyrosis, and eructation, but without epigastric pain. When younger, he observed that the ingestion of lobsters and crabs gave rise to nausea, vomiting, and diarrhea, and strawberries brought out an urticarial eruption.

On physical examination we see a man who has apparently lost weight, who is not anemic, whose breathing at the present time is good, although there is still some cough and expectoration. Today the lungs show little, but when he was seen for the first time in March this year there were sonorous and sibilant sounds and subcrepitant râles over the entire chest. In other words, there was a typical condition of bronchial asthma. Examination of the heart was negative, the blood-pressure slightly lowered, systolic being 110. The blood examination was as follows:

Leukocytes	9200	
Polys	68	per cent.
Eosinophils	4	"
Lymphocytes	28	"

Notice the very slight increase in eosinophils at the time of the first examination.

The abdominal examination was negative.

x-Ray examination of the paranasal sinuses and of the lungs was negative.

The tonsils are large, but apparently not infected. The teeth are in excellent condition.

Here, then, we have a typical case of bronchial asthma. Now, on the basis that this individual is suffering from repeated anaphylactic reactions, we must test him by means of the cutaneous reaction with various types of protein in order to discover the underlying cause. Let us take these up according to the outline which I have here upon the board.

I will introduce a few of the forms of protein which I have discovered give positive reactions in order that you may see for yourselves what these reactions are.

(Here the patient was given intradermal injections of horse epithelium and ragweed pollen as representative of the animal and vegetable emanations. Salt solution was introduced as a control.)

In addition to these two substances, the patient was also originally tested with the emanation of cat, dog, cow, and timothy and redtop pollens, to all of which the reactions were moderately positive with the exception of timothy, which was only slight.

Now I think at the end of perhaps three minutes you will see the striking contrast between the saline injection, which amounts to practically nothing, and the horse epithelium and ragweed pollen. The horse epithelium, which I should say is an extremely dilute solution, is giving a perfectly typical reaction manifested by the wide zone of hyperemia and the central urticarial wheal with the long pseudopod-like projection extending out into the hyperemic zone.

The ragweed test, as you see, is also positive, though it has by no means the same appearance of activity that characterizes the horse.

Food Proteins.—Next we must take up the study of food proteins. We have isolated the proteins from 60 of the commonest articles, including the meats, milk, eggs, fish, and other sea foods, vegetables, fruits, and some of the miscellaneous articles, such as coffee, chocolate, and nuts.

It is manifestly impossible to make all of these tests at one

time, and the number that can be made with safety at any time depends entirely upon the number that show a tendency to become positive. Too many tests given at once, causing reactions, will give rise to symptoms in proportion to the sum total of those that are positive.

In order to demonstrate the reactions of food proteins in the human, I will make the following tests:

Egg albumin.

Milk albumin.

Wheat protein (gliadin).

Beef protein.

(Here the intradermal injections of the above-named substances were given in the order named.)

On account of the fact that this patient is an excellent example of multiple sensitization—and you will remember that by "multiple sensitization" we mean a sensitization to many different types of unrelated proteins—I want to read you a list of the proteins to which he showed mild positive reactions: egg albumin, milk, chicken, bass, barley, sweet potatoes, whole wheat, cauliflower, celery, lima beans, peas, onion, beet, prunes, apple, oyster, clam, lobster, Postum, almond, rye, okra, mushroom, and mustard.

Now, let us look at our last series of four tests. The first, which is egg albumin, shows as marked a positive reaction as the horse epithelium. The milk albumin is also markedly positive. The wheat is more intense than the first two, whereas the beef has produced no appreciable change whatsoever.

Infection.—Now we come to the third group under specific causes, the foci of chronic infection. It is probable that these act as inciting causes by the absorption within the body of the bacterial proteins. In order to determine any such focus we must make careful examination of the nasal passages and paranasal sinuses, ears, tonsils, teeth. Chronic infections of the bronchial tract, gall-bladder, and appendix, as well as the genito-urinary tract will all be evidenced in a careful and systematic examination.

Bronchial asthma as a result of ethmoidal infections with

nasal polypi has usually been explained as a reflex action; whereas it is more than likely that the cures that result not infrequently from well-executed nasal operations are due to the fact that the infective focus is removed, or drainage is so established that bacterial absorption no longer occurs.

In the case that we have before us for study today it has been impossible to find any focus of infection other than a chronic infective bronchitis. A culture of his sputum showed two types of Streptococci viridans and a pure culture of pneumococcus was recovered after inoculation of a mouse.

In this particular case we do not have to consider the fourth of our specific causes, namely, subcutaneous or intravenous injections. In so far, then, as it is possible for us to go in the study of such a case, we can here make a diagnosis of bronchial asthma, and can demonstrate a sensitization to animal and vegetable emanations and food proteins, and have likewise determined a focus of chronic infection.

The important question then comes up as to treatment in a case of this type; what we can expect, or rather, what the patient can expect in the way of relief from symptoms after such a prolonged and careful study as to causes. In general, we can say that if we can completely separate a patient from any and all contact with those proteins to which he reacts, his relief will be assured. The only question comes in the management of those cases in which it is not possible to effect this separation. For example, in the present case. This man is in business in New York, and practically every time he comes to New York he has a marked exacerbation of symptoms. This is most noticeable on the streets, especially in the dust. The asthmatic attacks that ensue from such exposure are usually accompanied by mild hay-fever symptoms. Experience teaches that horse emanations are responsible for most of those cases developing symptoms under these conditions. It will be necessary, therefore, to treat this case with horse epithelium in order to desensitize him for the time being at least. It does not seem possible to explain the results that accrue from these inoculations, but we do know that a few injections apparently bring about an increased vasomotor

tone and permit the individual to overcome the persistent asthmatic tendency.

As far as the vegetable pollens are concerned, these will be discussed more in detail tomorrow under the subject of hay-fever itself, but as far as this particular case is concerned, I will merely say that if his business requires his appearance in and about New York during the time when these pollens are prevalent, then he should also receive injections against those proteins to which he has been shown to be sensitive.

The question of food proteins is oftentimes a difficult one to decide. In an instance like this, where an individual is sensitive to so many different types of foods, it would be manifestly impossible to attempt to desensitize him, and we must, therefore, accomplish results by dropping from the diet all those proteins to which he is sensitive. It is not possible, however, to make a hard-and-fast rule as to the duration of this restriction. Our patient has been deprived of all of these articles of food since the first of April. The most notable manifestation to him, after this restriction was established, was the complete disappearance of his digestive disturbance and constipation.

In cases like this I usually make it a rule to maintain the dietary restriction for a period of two or three months, and then, with the utmost care, gradually try out each separate article in order to determine whether or not there is a reappearance of any of the old trouble.

I want to impress upon you one fact right here. The presence of a positive cutaneous reaction does not necessarily signify that that particular protein when ingested will always give rise to symptoms. In a sense this is unfortunate, because we have no definite way of checking up our cases except by the use of combined clinical and experimental work.

On the other hand, I do not feel that this entirely vitiates our test, for we do know that the presence of such positive reactions is not normal. In general, the results of treatment based upon this line of study seem to yield more satisfactory results than were prevously obtained.

As far as the treatment for the foci of infection is concerned,

naturally these when discovered must be eliminated. Certain foci of infection, however, such as the one we are dealing with here, bronchial infection, are not directly get-at-able. Although the use of vaccines has in a certain sense been discredited, it is my firm conviction that they fill a very definite want in certain types of cases, and where the vaccines are autogenous and are made by competent bacteriologists, beneficial results can be accomplished. In this case, then, we use a vaccine containing the two forms of Streptococci viridans and one of pneumococcus in order to overcome the associated bronchial infection.

Again I must confess that bronchial infections stand in a rather different relation to bronchial asthma than most of the other types of infection, and it is not possible to say whether the infection acts anaphylactically or whether it is merely the mechanical interference with the entrance and exit of air due to a swollen and congested bronchial mucosa. There does not seem to me to be any way of definitely proving this at the present time. But whether the infection acts anaphylactically or mechanically, so long as it acts at all, it must be considered so far as the patient is concerned, and, therefore, in these cases we resort to the use of vaccines as the best method at present available.

This patient, then, has been receiving injections of horse epithelium, pollen extract, and vaccines. It is now two months that he has been under treatment, and let us see what improvement there is.

In the first place, he has no indigestion. He has gained in weight from 133 to 150 pounds. Although there is still some dyspnea after exertion, there is no asthma at all and he has been enabled to resume his work in town. The cough has diminished, the sputum has lessened in amount, and has changed from a purulent to a serious character.

As to the prognosis in this case, I can only, of course, speak from experience with similar ones. I know that after the injections of horse epithelium are stopped the patient will again in time become sensitive on exposure to horses. The same thing also holds true for the pollens. But if we can take a case of this sort and keep him free and clear from all asthmatic manifesta-

tions for a sufficiently long period of time, that is, three or four months, or possibly more in some cases, there seems to accumulate a sufficient degree of tone, let us say for lack of a better word, and although he may again develop asthmatic manifestations, he is likely to remain free and clear for months or years.

I do not want to overstate the possibilities of cure, nor do I want to underestimate them. The condition is under control the same as it is in those cases of tuberculosis that respond to treatment; we treat them, affect an arrest, and let them go; if they stay permanently arrested we consider it a cure. But because some of them have a recurrence it does not mean that treatment is not worth while. I think I may give you a little clearer idea of what I mean when I say that these cases still have the tendency to again develop their asthmatic attacks.

Tomorrow I shall take up the question particularly of hay-fever as a type of sensitization, and discuss very briefly also a few of the other clinical types, such as urticaria, angioneurotic edema, eczema, and chronic arthropathy.

HUMAN SENSITIZATION TO PROTEIN, AS EVIDENCED IN HAY-FEVER

This morning I wish to call your attention particularly to the question of hay-fever, or pollinosis, as it is now frequently called.

That pollens are the real cuse of hay-fever has now been conclusively proved, and particularly by this one fact, that the injection of a sufficiently large dose of a solution of a pollen protein into an individual who suffers from hay-fever will produce an immediate and typical manifestation of the affliction, no matter at what time of year the experiment may be performed.

It is not necessary to discuss now the question of whether the pollen is a toxin, as Dunbar has claimed, or whether the reaction is anaphylactic. Suffice it to say that it is generally conceded that the reactions are truly anaphylactic in nature, and this conclusion is based particularly on the fact that the injection of a solution of pollen protein into an individual not afflicted with hay-fever gives rise to no symptoms whatsoever. This would be entirely foreign to our conception of a toxin.

We can divide our cases of hay-fever into two separate groups: the so-called early hay-fever, which begins in the middle of May and lasts until the middle of July, and late hay-fever, which begins in the middle of August and lasts until October or heavy frost. I am speaking now of the period of onset and offset for this particular section of the country. Naturally, in the south and in the north the dates, while corresponding closely, are not identical.

Causes of Hay-fever.—Before taking up the clinical cases which I intend to present today I will enumerate briefly the pollens that have been discovered to be the most important factors in the disease.

Early Hay-fever.—In general, this is caused by the pollen of the grasses. In this section of the country the more important of the grammaceæ are called by their common names, timothy, redtop, June grass, sweet vernal, low spear, orchard grass, rye, wheat, quickgrass. In addition, the pollen of a few of the trees, such as the locust, chestnut, and maple, also the pollen of the daisy, rose, dandelion, honeysuckle, and privet are all responsible. But I want to impress most forcibly upon you the one fact that the grasses are the real factors in the causation of the typical disease as shown by the fact that practically all cases with a history of typical early hay-fever give decidedly positive cutaneous reaction to the grass pollens, whereas pollens of the other varieties mentioned are, comparatively speaking, infrequently positive.

As far as the grasses are concerned, we have shown that individuals with early hay-fever that react to one, react to probably all of the grasses, but with varying degrees of intensity. I must confess that I have been obliged to change my views as expressed in some previous publications, and I now believe that it makes a difference as to which of the forms of pollen we use, depending entirely upon the reactions obtained, and that those pollen solutions should be used which give the maximum reaction in any individual patient.

Late Hay-fever.—Of all the causes of late hay-fever, the pollen of ragweed stands first and foremost in importance. But in

addition, the pollen of goldenrod and certain of the late flowering grasses, aster, clematis, chrysanthemum, dahlia, and zenia give definite reactions in individual instances.

I will now present 2 cases for consideration, one a typical early hay-fever and the other a typical late hay-fever, and will verify the diagnosis of these cases and outline the treatment just as though I were seeing them for the first time myself.

The first case is one that has been under treatment for several years. The patient is thirty-seven years of age and has had hay-fever for ten years. It begins about the 20th to the 25th of May and lasts to approximately the 20th of July. The symptoms are typical, with nasal obstruction, nasal irritation causing sneezing and profuse discharge, and irritation of the eyes and throat. Toward the 10th of June a cough usually develops, oftentimes associated with some wheezing and occasional nocturnal dyspnea—in other words, a mild form of bronchial asthma associated with the hay-fever.

At other times of the year this patient's nasal and bronchial tract is perfectly clear and there are no complicating factors.

This year his treatment was begun on the 20th of March, approximately two months before the expected onset of the annual attack. At that time the cutaneous reaction was positive with pollen of the redtop grass and the ophthalmic reaction was also positive. Let me repeat these tests for you this morning in order to demonstrate exactly the manner in which they are carried out.

(Here the patient was given intradermal tests as follows:)

Intradermal:

Redtop grass,	0.1 mg. nitrogen per cubic centimeter.	Pos. moderate
	0.2 mg. nitrogen per cubic centimeter.	Pos. moderate.
	0.6 mg. nitrogen per cubic centimeter.	Pos. marked.
Timothy,	0.2 mg. nitrogen per cubic centimeter.	Pos. moderate.
	0.6 mg. nitrogen per cubic centimeter.	Pos. marked.
Ragweed,	0.6 mg. nitrogen per cubic centimeter.	Negative.

Ophthalmic:

Right Eye, Ragweed, 0.6 mg. nitrogen per cubic centimeter. Negative.
Right Eye, Redtop, 0.2 mg. nitrogen per cubic centimeter. Negative.

Left Eye, Timothy, 0.2 mg. nitrogen per cubic centimeter. Negative.
Right Eye, Redtop, 0.4 mg. nitrogen per cubic centimeter. Pos. sl. inj. and itch.
Right Eye, Redtop, 0.6 mg. nitrogen per cubic centimeter. Pos. marked, inj. and itch.
Left Eye, Timothy, 0.6 mg. nitrogen per cubic centimeter. Pos. moderate, inj. and itch.

As the result of these tests we can say with positiveness that this individual is sensitive to the grass pollens of timothy and redtop in practically the same degree. But I want to emphasize the absolutely negative reaction to ragweed, both cutaneous and ophthalmic, in as strong a concentration as 0.6 mg. of nitrogen per cubic centimeter. See how definitely this agrees with the patient's history of his trouble; he is not bothered in the slightest degree in August and September when the ragweed pollen is prevalent. This is as satisfactory a demonstration as can be given of the fact that these pollen reactions are specific and that the reaction is anaphylactic and not toxic. By that I mean it depends on the previously sensitized cells of the individual. The combination of the ophthalmic and cutaneous reactions gives us a fairly definite idea as to the degree of sensitiveness of the patient and therefore of the dose that is required and can be given with safety.

Mind you, the reactions that we obtained today are not identical with the reactions obtained in March when the patient was first tested this year, for at that time, though the cutaneous reactions were practically identical with that obtained today, the eye tests have changed, for at that time a solution of 0.2 mg. of nitrogen per cubic centimeter of both redtop and timothy gave definitely positive moderate reactions with corneal injection and marked itching.

This is an important point which must be borne in mind, for it shows the effect of the ten therapeutic injections which this patient has received up to the present time.

When we discover cases that give marked ophthalmic reactions with a solution of 0.1 or 0.2 mg. of nitrogen to the cubic centimeter the therapeutic dose must begin with a solution of

0.005 mg. of nitrogen to 0.01 mg. of nitrogen and be increased weekly about as follows:

2d injection (2d week) 0.02 mg. nitrogen
3d injection (3d week) 0.03 mg. nitrogen
4th injection (4th week) 0.05 mg. nitrogen
5th injection (5th week) 0.07 mg. nitrogen
6th injection (6th week) 0.10 mg. nitrogen
7th injection (7th week) 0.14 mg. nitrogen
8th injection (8th week) 0.2 mg. nitrogen
9th injection (9th week) 0.28 mg. nitrogen
10th injection (10th week) 0.4 mg. nitrogen
11th injection (11th week) 0.5 mg. nitrogen

From here on 0.5 mg. would be injected weekly up to the middle of July.

In this particular case the injections that have been given have reached 0.4 mg. nitrogen. At no time has there been a marked disturbance at the site of the injection after the first two treatments. It has seemed to me better, where weekly injections are given, to give all of them in approximately the same location in the same arm, for the local tissue immunity that occurs allows to give a larger dose with less local disturbance and with better constitutional benefit. Of course, where the treatments are given phylactically and necessarily closer together, this rule cannot be adhered to entirely.

So far this year, although it is now two weeks past the usual time of onset for the season, and a number of other cases that have not been immunized have been having symptoms for at least ten days, there have as yet been no symptoms of hay-fever whatsoever in this particular case.

I do not mean to say that I believe he will go through this entire season without being reminded that he has ever suffered from such a condition as hay-fever, for a large majority of these cases do have from time to time some suggestive evidence of their affliction so that they realize the season is at hand, but the treatment removes the greater part of the trouble (approximately 75 to 80 per cent.), so that the individual, although he has some symptoms, is able to continue his daily routine with little or no inconvenience.

As I stated at the beginning, this patient has been under treatment for three previous years. The first year was not entirely satisfactory. There was an underimmunization and only half of the trouble was removed. But the succeeding years have yielded better results, and, as near as can be estimated, about 80 per cent. of the trouble is relieved, and the asthma has not been a noticeable factor.

Case II.—The next case that I am going to demonstrate for you is one of late hay-fever. This man, thirty-three years of age, has had hay-fever since the age of five. I will write here on the board the reactions, cutaneous and ophthalmic, in such a way that our results can be noted as the tests are made.

(Scheme on board read as follows:)

Intradermal:

Redtop, 0.6 mg. nitrogen per cubic centimeter. Negative.
Ragweed, 0.2 mg. nitrogen per cubic centimeter. Positive, marked.
Goldenrod, 0.4 mg. nitrogen per cubic centimeter. Positive, moderate.

Ophthalmic:

Right Eye, Ragweed, 0.1 mg. nitrogen per cubic centimeter. Negative.
Left Eye, Goldenrod, 0.5 mg. nitrogen per cubic centimeter. Negative.
Right Eye, Ragweed, 0.2 mg. nitrogen per cubic centimeter. Negative.
Left Eye, Ragweed, 0.5 mg. nitrogen per cubic centimeter. Negative.
Right Eye, Ragweed, 1.0 mg. nitrogen per cubic centimeter. Pos. mod. inj. and itch.

This case has not as yet received any therapeutic injections. He is clearly and definitely a late hay-fever subject, as shown by the negative cutaneous reactions to redtop and also from his history, for he has no symptoms whatsoever until the middle of August.

Again, he is not an exquisitely sensitive case. In an instance like this the treatment injections would run about as follows:

First injection, about the middle of June, 0.02 mgm. N.
After one week, 0.04 mgm. N.
After one week, 0.08 " "
After one week, 0.15 " "
After one week, 0.24 " "
After one week, 0.35 " "
After one week, 0.5 " "

In such cases, as you see, after the sixth injection we are able to give approximately 0.5 milligram of nitrogen, all of these injections being given with little or no local and no constitutional reaction whatsoever, whereas in the former case all six injections amounted to only 0.1 mg. of nitrogen. In other words, the more highly sensitized an individual is shown to be, the less we are able to give without creating constitutional reactions. Further, the more sensitive an individual is, the less it seems to take to protect them. The probable explanation is that in the highly sensitized individual there is a greater chemical affinity and avidity between antigen and antibody. In all our treatments we aim to produce at first slight local reactions, which disappear within twenty-four or thirty-six hours, but no constitutional reaction whatever.

I merely cite these 2 cases as typical examples for your consideration, both from the diagnostic and therapeutic standpoints.

I am sorry I will not have time this morning to go into the question of prophylactic treatment. However, I may say that individuals who present themselves for treatment during their attack can be successfully managed with marked amelioration and oftentimes an early subsidence of symptoms. But the injections must be given at first daily and then at intervals of a few days, and the doses must all be correspondingly diminished.

As far as the results of treatment in hay-fever are concerned, I think we can summarize them briefly by saying that in 75 per cent. of our cases we are able to eliminate 75 per cent. of all symptoms. In this way we allow them to pass through their hay-fever season with comparatively little discomfort.

Another point that I might emphasize, as far as treatment is concerned, is that it is not permanent, and the injections, as far as is known now, must be given from year to year; although, as I intimated before, the results are better in the second year and in the third, at which time also the immunity is accomplished more easily and more completely.

I think I should express here a note of warning against the

careless use of this form of treatment. In certain cases, and particularly in those in which there is an asthmatic tendency, an overdose can produce violent constitutional disturbance, and it is conceivable that anaphylactic shock with death could occur here in just the same way that it has occurred in those cases sensitized to horse-serum that have received immunizing or therapeutic doses of diphtheria antitoxin in horse-serum.

OTHER CONDITIONS OF SENSITIZATIONS

As far as the other clinical conditions that are mostly anaphylactic are concerned, I shall have to speak with great brevity.

Next to hay-fever, the most prominent clinical condition of sensitization is that involving the gastro-intestinal tract. There are different forms. The symptoms may consist of swelling of the legs, the tongue, and the glottis as soon as a certain type of protein is introduced into the mouth. Or the symptoms may be those of vomiting with intense epigastric pain when the stomach itself is sensitive. This condition is usually followed by abdominal pain, colicky in type, and profuse purging.

Of the food proteins usually responsible for this I might mention egg, milk, fish and shell-fish, meat, and fruit, especially strawberries, in the order named.

It is not, however, those cases in which violent symptoms ensue immediately on the ingestion of food that concern us mostly, for these are usually readily recognized and avoided, except in infants that are artificially fed or in those to whom the mother's milk is poisonous. It is in that group in which the symptoms are more indefinite and vague, rather those of indigestion, in which our best results, I believe, are going to be obtained. For it is in this group that the diagnosis has to be made for the patient by means of the cutaneous, sometimes even the ophthalmic, reactions.

As far as treatment in these cases of sensitization is concerned, I do not hesitate to say it is at least unsatisfactory, whether it is pursued by means of minimal doses of the protein by mouth or by hypodermic injections. Complete avoidance of the food is,

by all means, the most satisfactory, although in a few cases the preliminary treatment by hypodermic injection, followed by the continued ingestion of this form of protein has apparently yielded satisfactory results.

Urticaria.—This is undoubtedly in many cases an anaphylactic reaction. But from the large number of cases that I have studied, it has not seemed possible to determine by means of cutaneous reactions the particular form of food protein to which they are sensitized. I should say that tests in only about 50 per cent. of our cases have yielded satisfactory results.

Angioneurotic Edema.—This is undoubtedly an anaphylactic reaction in which the sensitized cells are those connective-tissue cells of the subcutaneous tissues in contrast to the epithelial cells sensitized in urticaria. The discovery of the underlying specific cause in these cases has been made in probably not more than 25 per cent. of those investigated.

Chronic Joint Disease.—Lately there has been considerable discussion with regard to the anaphylactic nature of certain types of arthropathies, especially the so-called hypertrophic arthritis. I have investigated, up to the present time, only 6 such cases, using the entire group of food proteins available, and in none of these instances have I discovered any reaction that seemed to me to warrant the conclusion that there was any etiologic relationship whatsoever.

Eczema.—This is another condition that has been and is being studied from the anaphylactic basis. While it is true that these cases seem to be particularly common in those families in which there is a history of protein sensitization of one form or another, I have not yet been able, in a series of 15 cases studied, to obtain any information that warrants the belief that this disease is in itself anaphylactic in type. Of course this, as well as the former group, must be studied on a broader scale until we are able definitely to include or exclude them from the group of protein sensitizations.

It is not possible in a discussion such as this to give you more than a brief résumé of this tremendous field of protein sensitizations. But I trust that I have given you a clear conception of

some of the fundamental points and a definite idea of our present-day limitations which open a splendid field for investigation and study. I am also compelled to say that I should feel that our two-hour lecture had been entirely wasted if I have not stimulated and aroused in you an interest that will compel your co-operation in the further development of this comparatively new subject in medicine and therapy.

CLINIC OF DR. WALTER L. NILES

BELLEVUE HOSPITAL

MENINGITIS. THREE CASES: TWO OF MENINGOCOCCIC AND ONE OF STAPHYLOCOCCIC ORIGIN

Demonstration of Patients; Discussion of Diagnosis and Treatment, with Special Reference to Administration of Flexner's Serum.

April 20, 1917.

DR. NILES: We have recently had several unusual and instructive cases of meningitis in our wards, and I am going to present 3 of them today. One is still quite ill and we will have her brought in first.

CLINICAL CLERK: The patient is a school-girl, eleven years of age. She was admitted to the hospital on April 11th, at 5 P. M., in a stuporous condition. Her father, who brought her here, says that she was perfectly well until the day before admission, when she complained of headache which was apparently not very severe. The morning of admission she was feverish and wanted to lie down. At 2 P. M. she vomited "very suddenly," and soon became unable to speak or recognize anyone. She had no convulsions; no nose, ear, or throat symptoms, and, so far as known, had not been exposed to meningitis. Her bowels have not moved since the onset of her illness.

Family History.—Negative.

Past History.—Measles, pertussis, pneumonia, and scarlet fever when quite small. No complications or apparent sequelæ.

DR. NILES: What was the temperature, pulse, and respiration on admission?

CLINICAL CLERK: Temperature, 103.6° F.; pulse, 120; respirations, 36.

Dr. Niles: What was the location of the headache?

Clinical Clerk: Her father said that on the first day it was frontal, but that night and the next morning it was at "the base of her brain."

Dr. Niles: We have, then, the usual symptoms of the onset of meningitis, viz.: headache, soon becoming occipital and very severe; fever; sudden vomiting, so-called cerebral or projectile, and constipation. The slow pulse which is usually mentioned in descriptions of the infection was, however, not present, and upon referring to her chart you will see that it at no time became notably slowed. The irregularity of this symptom in different cases I am not able to account for. The usual explanation offered, that it depends upon the degree of intracranial pressure, does not always hold. It seems to vary in different epidemics. In the epidemic of 1904–05 I saw many cases with pulses down to 60 or lower at the onset of the disease, but very few of our cases in recent years have developed this symptom. Another variable symptom is herpes. Has this patient any?

Clinical Clerk: No. She has had none.

Dr. Niles: The eruption is often very extensive on the lips, alæ nasi, face, and ears. I believe this, too, is more common in the epidemics of the disease than in sporadic cases, and I want to emphasize the fact that the absence of these symptoms—slow pulse and herpes—does not tend to eliminate the diagnosis of meningitis. Their presence, however, is of considerable importance in suggesting such a diagnosis. Please proceed with the physical findings.

Clinical Clerk: Patient was well developed and well nourished. Was unconscious and her breathing stertorous.

Eyes: Slow, lateral nystagmus to right. Pupils, right in mid-dilatation; left, contracted. Neither react to light. The fundi showed beginning optic neuritis in the right; left, normal.

Mouth: Constant gnashing of teeth.

Neck: Moderately retracted and very rigid.

Heart and lungs: Negative.

Abdomen: Wall firmly contracted. No viscera or masses felt.

Extremities: Right arm somewhat spastic and moved less freely than the left. Right hand held in accoucheur's position. Legs held firmly in partial flexion.

Knee- and ankle-jerks not obtained.

Babinski's sign present on the right side; suggestive on the left. Brudzinski's sign present.

Very marked Kernig's sign in both legs.

Skin: No eruption. Marked dermographia.

Leukocytes, 28,600; P. M. N., 95 per cent.; S. M., 5 per cent.

Urine: Negative.

Dr. Niles: This was evidently a very rapidly spreading infection extensively involving the leptomeninges. Were her ears, nose, and throat carefully examined?

Clinical Clerk: Yes, and were normal. A culture from the nose showed only *Staphylococcus aureus.*

Dr. Niles: How was the exciting cause of the meningitis identified?

Clinical Clerk: By lumbar puncture at 5.30 p. m. The spinal fluid was under increased pressure, cloudy, contained 5000 cells per cubic millimeter, all polymorphonuclears. Gram-negative cocci were seen in large numbers, both intra- and extracellular; 25 c.c. of fluid were removed and 20 c.c. of anti-meningococcic serum injected by the gravity method.

Dr. Niles: Was the serum injected at the first puncture, that is, before the fluid was examined?

Clinical Clerk: Yes.

Dr. Niles: That was right. Under such conditions the serum should always be given at once. Do not wait to examine the spinal fluid. Was a blood-culture made?

Clinical Clerk: Yes, two. They showed no growth.

Dr. Niles: By referring to the chart you will note that ten doses of serum were administered within five days, 20 c.c. being the amount given each time except twice, when 30 c.c. were injected, and once only 5 c.c. because of defective apparatus. An eleventh dose of 20 c.c. was given on the ninth day of her illness. Notice the number of cells present in the various tappings and especially the recent marked reduction in their number.

I may say that the tappings and subsequent injections of serum were often laborious and time-consuming procedures. Two hours were sometimes required, and if this girl recovers, as now seems probable, she may well thank Dr. Flexner for perfecting the

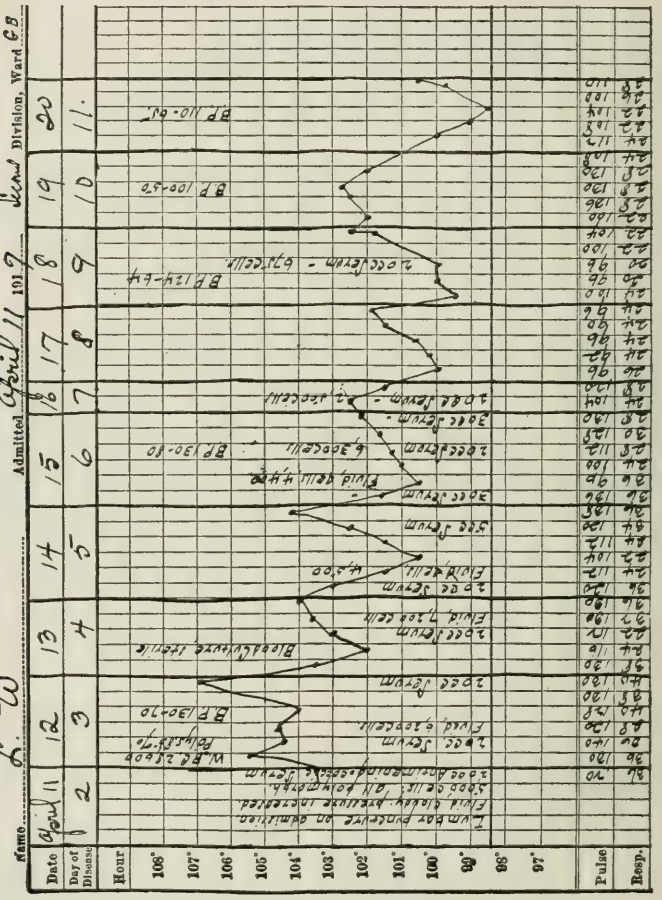


Fig. 66.—Chart in Case I.

serum, and the house staff for their devotion in administering it and thereby saving her life, for quite surely she would not have recovered had this infection developed only a few years ago. What has been the course of her symptoms?

CLINICAL CLERK: April 12th. Patient conscious; very restless and irritable. Eyes rotated to right; pupils equal, widely dilated; react very little to light. Spinal fluid under very marked pressure. Neck rigid, abdomen retracted, and spine in moderate opisthotonos.

April 13th. Opisthotonos more marked. Conscious, and complains of pain in back of neck and down spine. General hyperesthesia. Double Kernig and right Babinski persist.

April 15th. Little change in signs. Spinal fluid under less pressure and shows fewer cells.

April 17th. Neck and spine less rigid. Spinal fluid only slightly turbid and under little pressure; 3500 cells.

April 18th. Appears distinctly better. Has less pain and hyperesthesia and can lie almost flat on the bed. Neck is still very rigid, but not much retracted. Bilateral Kernig's sign present. Pupils are widely dilated, but equal, and react moderately to light. She has no palsies. Spinal fluid contains 675 cells.

April 19th. This morning fever higher and does not feel as well. Had two spots of urticaria on her neck. By noon the eruption had extended all over her body and her eyes were almost closed. There was intense itching.

Blood-pressure, 100–50, the systolic pressure having fallen 30 mm.

DR. NILES: How long since the first injection of serum?

CLINICAL CLERK: Nine days.

DR. NILES: What is the nature of her present condition?

CLINICAL CLERK: It is serum disease, evidencing the sensitization of her cells to horse-serum. It is an anaphylactic phenomenon.

DR. NILES: Yes. Doubtless so. Have you counted her leukocytes or determined the coagulation time of her blood?

CLINICAL CLERK: No.

DR. NILES: They should be done. An eosinophilia, often high, is usually found. Dr. Weil tells me that there is also always a delay in the coagulation time of the blood. In one of our cases it was delayed to fifteen minutes.

Serum disease is one of the few sequels to the use of the serum, and occurs in about one-third of the cases. It develops eight or ten days after the first injection and is manifested by the symptoms here noted. I believe this patient also has joint pains, which are a common symptom. The important point is not to mistake it for an exacerbation of the infection and give more serum. This should be avoided, for, if done, the meningitic symptoms will quite surely increase temporarily, or if several days have elapsed since the last injection, there is danger of anaphylactic shock.

The improvement in this patient's general condition has been so marked and her spinal fluid has cleared to such a degree that it is quite probable she will now proceed to a complete recovery. Yet meningococcic infection is so irregular in every symptom and so treacherous that she may suffer a relapse or gradually develop subacute serous meningitis. These are, however, rare occurrences when the serum is administered early in the disease and adequately.

The development and use of Flexner's antimeningococcic serum marks one of the few great therapeutic achievements of the past decade. During the epidemic of 1904–05 the mortality in New York City was 70 per cent., and it was unusual for patients to escape without some serious sequel, such as paralyses, loss of hearing or sight, or mental impairment. Now with the serum the figures are reversed and recovery is usually complete. When the administration is begun within twenty-four hours of the onset the mortality is only 18 per cent., which emphasizes the importance of early diagnosis and treatment. The amount of spinal fluid withdrawn should always be somewhat more (5–10 c.c.) than the amount of serum injected. The average dose for an adult is 30 c.c., but in very severe cases from which the fluid escapes readily as much as 60 c.c. may be given. The usual frequency of administration is once in twenty-four hours until the temperature is normal and the fluid practically clear, but we have gradually come to give it at twelve-hour intervals in severe cases, and have occasionally given it every six hours on the first day of treatment. The aim is to keep a high concentra-

tion of the serum continuously in the subarachnoid space, so when in doubt regarding repetition of the dose it is safer to give the serum very frequently. The average case requires only four to six doses, but severe infections, especially when treatment is commenced late, require many doses. You will notice that the number of cells in the spinal fluid was greater after the first dose. This is usual and is due to irritation of the meninges by the horse-serum. It is, however, transitory and the fluid will clear. If there is a bacteremia, about 50 c.c. of serum should be given intravenously. In this case the blood-cultures were sterile.

The dangers accompanying intraspinal injections of the serum are very few, but should be kept in mind. Anaphylactic shock has been mentioned, and is to be avoided by giving a sensitizing dose subcutaneously before proceeding with the intraspinal injection. Occasionally respiratory or cardiac symptoms develop during the injection. In such an event stop it at once and drain off a few cubic centimeters of serum. If necessary do not hesitate to make another puncture for draining off the fluid. Also do artificial respiration and give circulatory stimulants. This accident is most unusual when the serum is introduced by gravity, which is the method to be employed. Are there any questions?

STUDENT: Where can the serum be obtained?

DR. NILES: It is of the greatest importance to have a serum which is polyvalent and of high potency. Some commercial houses have, unfortunately, not manufactured such sera, and standardization is now contemplated by the government. Here in New York we prefer that made by the laboratories of the Department of Health.

Subsequent Course of the Case.—The temperature continued to be slightly elevated for two days, when it became normal. Her blood showed 16,000 leukocytes with 12 per cent. of eosinophil cells. The coagulation time was nineteen minutes. Her recovery was uninterrupted except that her heart rate continued at about 100 for three weeks. She left the hospital on June 1, 1917, cured.

DR. NILES: The next case puzzled us greatly for several days, but the outcome and response to treatment quite definitely classify it.

CLINICAL CLERK: The patient is a colored woman who was born in the West Indies. She is thirty-eight years of age, married, a laundress by occupation. She was admitted to the hospital on March 29, 1917, complaining of dizziness, poor vision, and pain in her head and small of her back.

The present illness began on March 15, 1917, with dull pain in her lumbar region. A little later she began to have headache which was constantly severe and referred to the occipital region. She thinks she then had fever which has continued to the present time. A physician who was called said she had kidney trouble and ordered hot applications to her back, which gave relief. A day or two after the onset she began to have dizziness which made her very uncomfortable when she raised or moved her head. Vision has been impaired since March 23d, objects are blurred, and she is unable to read. There have been no convulsions, paralyses, or delirium. She has had no cough, dyspnea, or edema. Her bowels never move without a cathartic and she has been constipated throughout this illness, but not more so than usual. Her complaint is chiefly of headache.

Family History.—Negative for cancer, nervous diseases, and tuberculosis.

Past History.—She has never been sick since childhood, when she thinks she had mumps. Is not subject to colds or sore throat and was perfectly well until the onset of this illness. Venereal diseases are denied. Her husband is living and well. She has one healthy child three years old. One died at nineteen years; cause unknown. Has had three miscarriages, the dates and duration of pregnancy not remembered. She has lost no weight and has never had pleurisy or hemoptysis.

On admission her temperature was 102.4° F.; pulse, 72; respirations, 24.

DR. NILES: The patient, then, is a married colored woman who was born in the West Indies and who, aside from three miscarriages, has been remarkably well and strong until the on-

set of this illness. She has lost no weight nor has she had any other symptoms of tubercle infection; neither is there any history of tuberculosis in her family. The history as related implies a rather gradual onset, but I am inclined to think she was suffering quite severely; otherwise a physician would not have been called. Headache, mostly occipital, has been the predominant symptom, accompanied by less severe pain in her lumbar region, fever, dizziness, and dimness of vision. These symptoms have continued for two weeks without notable change. Vomiting was not mentioned.

CLINICAL CLERK: She has not vomited.

DR. NILES: From the history we can only say that it suggests an acute infection with the cranium as the seat of it, but the symptoms might be those of a general infection. Headache rarely lasts for two weeks in typhoid fever, nor is it often occipital in location. Severe headache, sometimes occipital, is constant in typhus fever, and it is usually the predominant complaint throughout the course. We have several such cases every year, as the disease is endemic in New York. I have never seen or heard of a case in a colored person, however. Consideration of the physical findings will put us on the right track.

CLINICAL CLERK: On admission she was poorly nourished, though not emaciated, and did not look acutely ill.

Skin: Dry and rough. No eruption or dermographia.

Ears and throat: Negative.

Eyes: No extra-ocular defects. Pupils moderately dilated, regular in outline, and react promptly to light and accommodation. Eye-grounds normal. This was confirmed by Dr. O'Connor, resident surgeon on the ophthalmologic service.

Nose: Negative except for a small patch of herpes on the septum.

Mouth: Tongue heavily coated and dry; not tremulous. Teeth in poor repair, surrounded with pyorrhea and covered with sordes. Pharynx negative.

Neck: No palpable glands. Neck slightly stiff to forward movement; not retracted or limited in motion backward.

Chest: Heart and lungs negative.

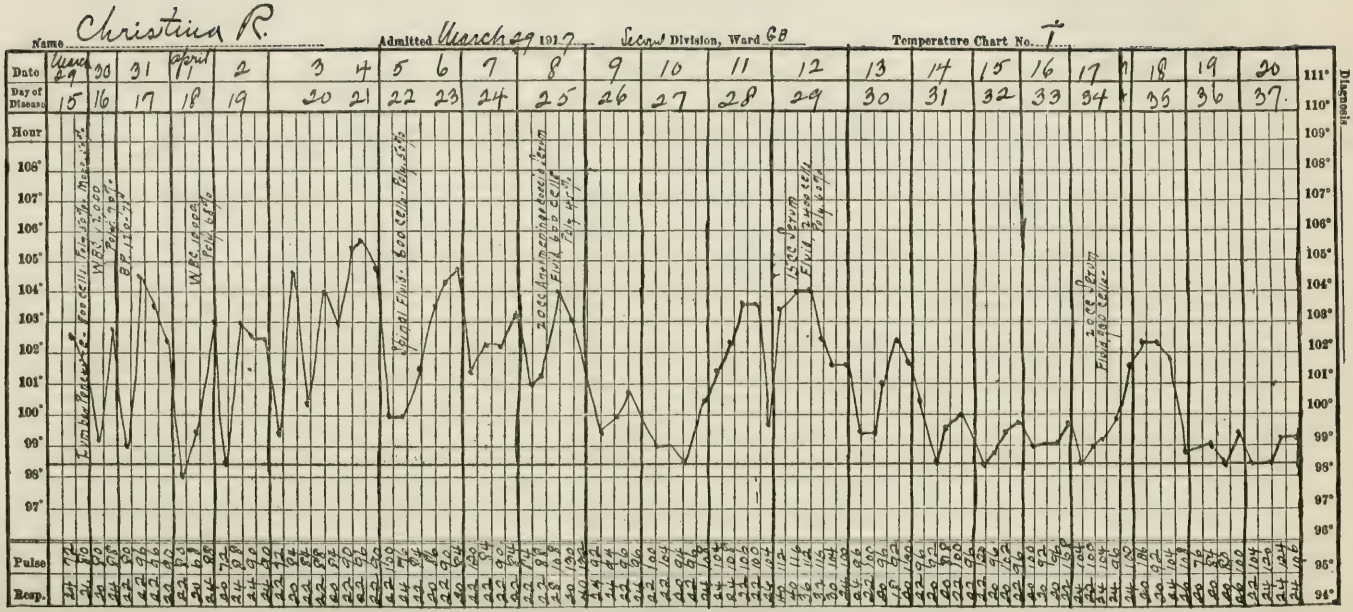


Fig. 67.—Chart in Case II.

Arteries: Easily palpable, not tortuous. Blood-pressure 120–75.

Abdomen: Symmetric, flat, but not retracted. Viscera not palpable.

Extremities: No paralyses or disturbances of sensation. Skin reflexes present and equal. Knee-jerks present and equal, but diminished. Also the ankle reflexes. No Kernig, Babinski, Oppenheim, Gordon, or Brudzinski signs.

Blood examination March 30, 1917:

W. B. C., 12,000.
P. M. N., 70 per cent.
P. M. E., 2 per cent.
S. M., 21 per cent.
L. M., 4 per cent.
Trans., 3 per cent.
R. B. C., 5,200,000.
Hb., 95 per cent.

Urine showed a trace of albumin and a few granular casts. No pus or bacteria. Another blood examination on March 18th showed leukocytes 10,000, with 68 per cent. of polymorphonuclear neutrophils, and 17 per cent. small mononuclears.

Dr. Niles: The physical examination did not reveal conclusive evidence of any specific disease. She was not well nourished and even now looks somewhat emaciated, I think. You see that tapping the muscles with a percussion hammer brings out clearly defined swellings at the point of irritation which last for a few seconds and then disappear. These are called myoidemas and are a certain indication of wasting of the muscle. They are commonly very marked in tuberculosis, but, I think, are just as constant, though usually not so large, in all other states of general or local impairment of nutrition. So, despite her history, I believe she has lost considerable flesh. On admission, then, her cerebration was normal. She had a dry tongue, which always indicates a severe degree of toxemia, except in persistent mouth-breathers, and she had emaciated. Her neck was slightly rigid and her tendon reflexes were depressed,

but she had no palsies or other signs of localized intracranial pressure. A small patch of herpes was on her nose.

(To a student): Mr. Brown, what conditions suggest themselves to you to explain such a state?

Mr. Brown: Meningismus complicating typhoid fever, or perhaps uremia.

Dr. Niles: In regard to the latter it is true there were albumin and casts in the urine, but they are practically always present in fevers of this duration; besides, there was no hypertension, her eye-grounds were normal, and she had no hyperpnea. I think we could safely eliminate uremia at once. The picture was very much like meningismus though, and we at first thought that was the condition. The neck stiffness is usually moderate and without retraction except in children. Kernig's sign is usually present, but not always, and the reflexes are apt to be more active than normal. Did she have typhoid fever? Probably not, because the headache had lasted two weeks and was occipital, the spleen could not be felt, and there were no rose-spots. They are sometimes difficult to see in colored people, it is true, but a good light brings them to notice. Her pulse was slow in proportion to the fever, which may be the case as late as the end of the second week, but it was not dicrotic as it usually is even at this period of the infection. Her blood did not show leukopenia, but at the present time we have 2 cases of typhoid fever which some of you have seen, one with 16,000 and the other with 12,600 leukocytes. These counts were not made after a bath either, for we rarely give any hydrotherapy in typhoid fever except two cleansing baths daily. Obviously, the next step in our diagnosis was to determine if we were dealing with meningismus. How was that done?

Clinical Clerk: By lumbar puncture. The fluid was distinctly cloudy and ran very freely. Examination showed 800 cells per cubic millimeter, 50 per cent. being polynuclears and 50 per cent. mononuclears. Noguchi test positive. Fehling's solution was reduced. No bacteria were found in the smears and cultures were sterile.

Dr. Niles: It was then clear that there was inflammation

of the meninges. The cells are sometimes much more numerous than normal in meningismus, but not to this degree, and they are practically all lymphocytes. What infection does such a spinal fluid suggest to you?

CLINICAL CLERK: Tubercle infection, though the number of cells is usually not so large and lymphocytes predominate.

DR. NILES: Yes, that is a very high count for tuberculous meningitis, but I have seen it in children. It is true that mononuclear cells usually predominate, but sometimes polynuclears are in the majority. Was the fluid carefully and properly searched for tubercle bacilli?

CLINICAL CLERK: Yes. Dr. Cecil and several clerks spent a great deal of time on this fluid and three later tappings without finding any organisms.

DR. NILES: That should have been given more weight than we ascribed to it at the time, for such study almost invariably reveals the tubercle bacillus if it is present. Was a guinea-pig inoculated?

CLINICAL CLERK: Yes, and is still alive.

DR. NILES: I think the necropsy will reveal only normal tissues. We were all mistaken about this case. Here was a colored woman with a meningitis which developed quickly and gave a spinal fluid as described, and we concluded that it must be tuberculous in origin. To be sure, she was thirty-eight years old, gave no history suggestive of tubercle infection, and no lesions could be determined on examination. The radiograms of her lungs, as you can see, show nothing even suspicious. Careful searches failed to identify the bacillus in the spinal fluid. Tubercles in the choroid were, of course, not present. They very rarely aid the diagnosis except in the text-books. These are all reasons why we should have declined that diagnosis.

Other findings were: blood-cultures negative; Widal reactions negative; Wassermanns of blood and spinal fluid negative; cultures of urine and spinal fluids negative.

You will notice her temperature continued to be high, her pulse was generally slow, and there was little change in her general condition. On the third day after admission weakness

of the left sixth cranial nerve was evident, the first and only evidence of localization which she presented. That has cleared up after lasting twelve days.

As you know, Dr. Cecil has this past winter been intravenously injecting a variety of foreign proteins in several forms of infection, especially acute rheumatic fever. He was greatly interested in this woman throughout, and one day suggested to me that he give her some horse-serum intraspinally with the view of securing the leukocytic and perhaps phagocytic reaction produced by serum. I readily agreed, particularly as she seemed to have surprisingly good resistance to tubercle infection. We thought our best available form of horse-serum for the purpose was antimeningococcic serum, and accordingly she was tapped and 20 c.c. injected on April 8th. You can best follow the result by her temperature chart. Notice that the next tap showed 2400 cells, the usual reaction to serum. She received only three doses of serum, as we began it half-heartedly and did not know what to expect, but the woman is today practically cured. She has no pain, her neck is not stiff, and her eye has returned to normal. Of course, we have not cured a case of tuberculous meningitis, but we have cured a meningococcus infection. Doctors Josephine Neal and Phebe L. DuBois of the Health Department have both seen the case and agree that it was cerebrospinal fever. They tell us that after a week or two it is often impossible to find the organisms in the spinal fluid and the process becomes a low-grade inflammation with serous exudate predominating and little cellular reaction.

This case also emphasizes the fact that when in doubt regarding the nature of a meningitis it is best to give the antimeningococcic serum.

Further Course of the Case.—Recovery was complete and uneventful. Discharged May 6, 1917, cured.

The patient who is now walking in has been exceedingly ill and has had meningitis, though it was an incident in the course of a general infection. He has now almost completely recovered and is going home today.

CLINICAL CLERK: The patient is a colored man, forty years of age, a longshoreman by occupation, who was admitted to the hospital on February 23, 1917, complaining of numbness in his left leg and pain in his dorsal spine.

Present Illness (history obtained from friends).—The patient was well and at work on February 16, 1917, when he suddenly lost consciousness. This lasted for two days, after which he appeared to be much better until the day of admission, when he became delirious and could not be controlled. Since the onset he has at times complained of some stiffness of his neck and motion has caused severe pain. He has also had headache, which has been chiefly occipital in location. He now complains of a numb feeling in his right arm and leg and some pain down the posterior aspect of his left leg. There is also a dull aching pain throughout his spine, but mostly in his dorsal region. He has not vomited since the onset and has had no convulsions. His friends think he has had fever since the onset of his illness.

Family History.—Father living and well. Mother died of tuberculosis at about twenty-five. Five brothers and three sisters living and well. Two died in infancy, cause unknown.

Past History.—Had measles and malaria in childhood. Pneumonia in 1902; complete recovery. Last December he froze the third and fourth fingers of his right hand, and they have never entirely healed, the third finger being worse than the other. He has had no cough, hemoptysis, or loss of weight. Appetite good. Bowels regular until the present illness, since when they have been constipated. Has had gonorrhea twice; lues is denied. Has been a heavy drinker of whisky since his youth, and during the past several weeks has been very nervous and shaky.

DR. NILES: A history such as you have recounted strongly suggests alcohol as the cause. Most of the illnesses which we see here are modified by that poison. The histories are apt to be confused and unreliable and wide-spread pains are frequently complained of. Delirium is, of course, a common enough manifestation of alcoholic poisoning, and it is quite probable that the course of this man's infection has been masked by chronic

alcoholism. It is, however, perfectly evident that he had a more serious condition as well. What were the physical findings?

Clinical Clerk: The patient was a large, well-nourished and well-developed colored man. He did not appear very acutely ill, though he was disoriented and confused. He lay quietly in bed often muttering to himself.

Neck: Distinctly rigid and slightly retracted. The entire spine was firmly held.

Eyes: Pupils irregular in outline, the left being larger than the right. Both react to light and accommodation. No exophthalmos, nystagmus, or extra-ocular palsies. There was a slight right conjunctivitis.

Ears and nose: Negative.

Tongue: Heavily coated, protruded in the midline, slightly tremulous, moist.

Teeth: In poor condition. Gums show pyorrhea.

Tonsils: Moderate size, moderately congested, as was the pharynx also.

Heart, lungs, and abdomen: Negative.

Extremities: Distal phalanx of the third and fourth fingers of the left hand have been partially amputated. There is a bluish discoloration and diminished external heat over the remaining portions of these phalanges. The bone protrudes through the flesh of the third finger and is surrounded by crusts under which there is a little pus. No edema. No weakness or paralyses.

Reflexes: Knee- and ankle-jerks normal. No Babinski, Oppenheim, or Brudzinski. No clonus. Well-marked bilateral Kernig's sign present.

Blood count: Leukocytes, 18,000. P. M. N., 88 per cent.

Urine showed a marked trace of albumin and a few granular casts.

Dr. Niles: The physical findings which you have described, viz.: delirium, unequal pupils, stiff neck, and Kernig's sign, together with leukocytosis, of course demand a lumbar puncture. Please describe the fluid obtained?

Clinical Clerk: It was a blood-tinged, purulent looking fluid under increased pressure. Microscopic examination showed

1500 cells per cubic millimeter, 99 per cent. being polymorphonuclears. Globulin in excess. No bacteria seen.

Dr. Niles: The fluid was quite thick and looked as if it contained more than 1500 cells. One rarely fails to find the meningococcus on staining a smear when the fluid is very cloudy in cerebrospinal fever, but we assumed we were dealing with a meningococcus infection, and on the first puncture injected 20 c.c. of Flexner's serum, having withdrawn 25 c.c. of spinal exudate. Cultures were made from the fluid and a blood-culture was shortly taken. Intraspinal injections of serum were repeated at frequent intervals, as shown on the chart. The spinal fluid continued to be very cloudy and was always tinged with blood. Please note that on the day after the first spinal injection the cell count had risen to 5000, the usual reaction to horse-serum. No bacteria were discovered in the smears, and it was with surprise and a certain degree of incredulity that we received Dr. Guion's report of the growth of *Staphylococcus aureus* from the spinal exudate. We nevertheless continued giving the serum, though the patient showed no improvement. In fact, he became more delirious, but it was the alcoholic type, and he apparently had delirium tremens. On the fourth day in the hospital Gram-positive cocci were found in smears from the spinal tapping, and to add further interest to the case Dr. Guion reported the growth of *Staphylococcus aureus* from the blood. We were, therefore, dealing with a staphylococcus septicemia as well as meningitis, but it was not clear whether the latter was primary or secondary. The chart shows that we continued to administer the antimeningococcus serum, though, of course, its specific properties were of no avail, but I hoped that the reaction produced in the leptomeninges by the foreign protein would be beneficial and, besides, we have no specific means of combating such an infection.

The patient developed no new symptoms, but all of the former ones persisted and it was necessary to restrain him until March 2d, when his mental condition became clearer, the temperature and pulse lower, and the spinal fluid less cloudy, showing only 440 cells per cubic millimeter., 40 per cent. of which were poly-

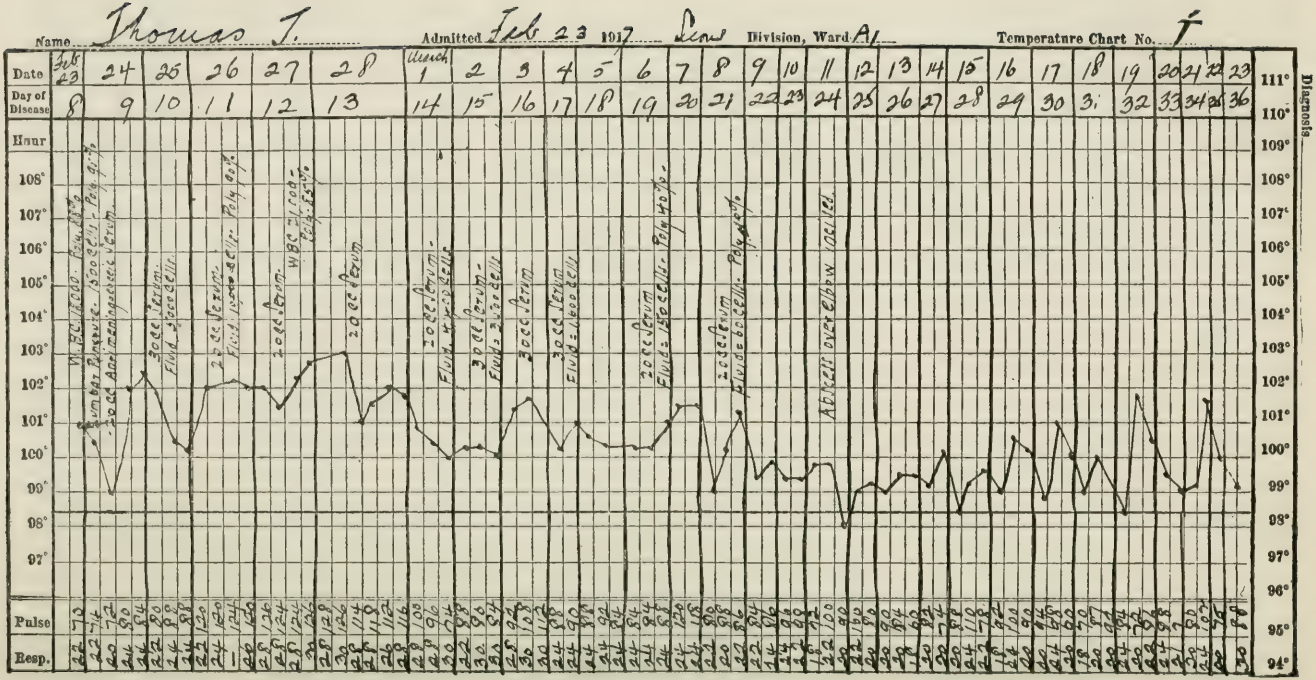


Fig. 68.—Chart in Case III.

morphonuclears and 60 per cent. mononuclears. Improvement was now progressive and on March 8th he was perfectly rational

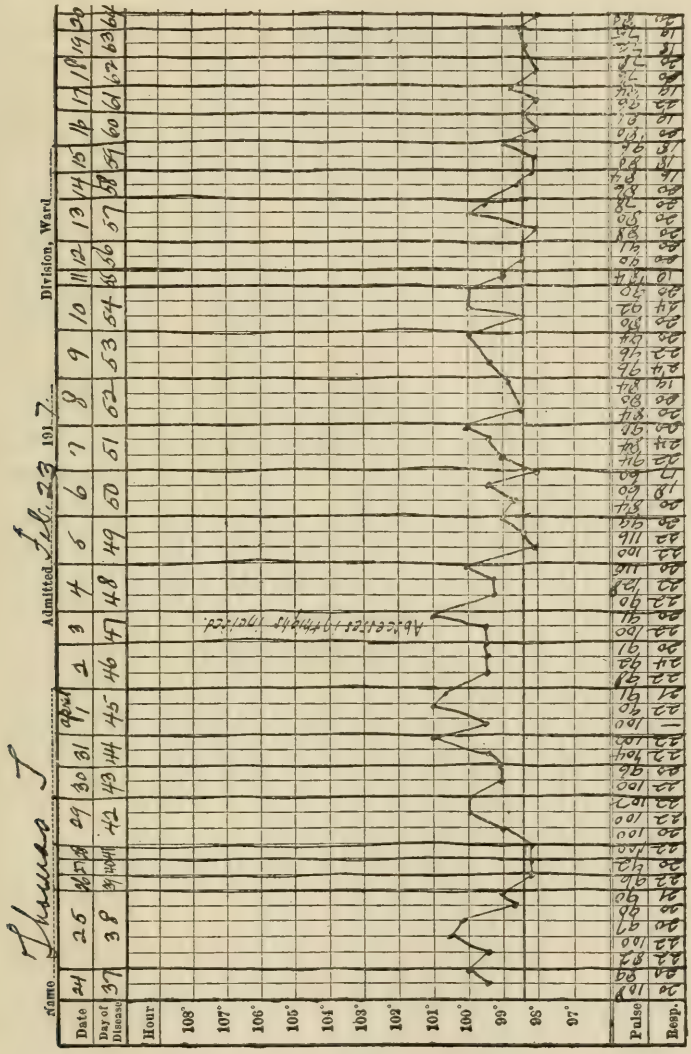


Fig. 69.—Chart in Case III (continued).

and comfortable. His neck was slightly rigid, and Kernig's sign remained, but there were no other neurologic signs. His tap was clear and gave only 60 cells per cubic millimeter., 10

per cent. being polymorphonuclears. A blood-culture taken on March 5th remained sterile. Wassermann tests of the blood and spinal fluid were negative.

During the course of his struggles to escape from restraint the skin over his left elbow became abraded, and on March 9th redness and swelling with fluctuation over the joint was noted. This was then regarded as a local infection and we were not surprised to find *Staphylococcus aureus* in the cultures from the pus evacuated when the abscess was incised under local anesthesia. The infection fortunately did not involve the elbow-joint. He then continued to improve until March 29th, when he had a little fever and complained of pain on the inner side of his right thigh. These symptoms continued, and on March 31st it became evident that there was an abscess beneath the adductor muscles. At this time similar signs presented themselves in the same part of the left thigh. He was then anesthetized, and Dr. Blythe evacuated a large quantity of pus from the right thigh and a small amount from the left, from which cultures gave pure growths of *Staphylococcus aureus*. Since then his convalescence has been uneventful and you now see the man perfectly well except for these small drainage openings in his thighs. He is going home today, having been directed to return to the Out-patient Department for subsequent dressings. He has, therefore, had a purulent leptomeningitis, bacteremia, and multiple abscesses, all of *Staphylococcus aureus* origin. Now these must have been secondary to some focus of *Staphylococcus aureas* infection. Have you found such a focus?

Clinical Clerk: Yes, in this frozen finger. There is a low grade of osteomyelitis and *Staphylococcus aureus* has been cultured from it.

Dr. Niles: So this so-called "frost-bitten" finger assumes great importance. I think it is safe to say that this was the atrium for the infection which resulted in bacteremia first, then meningitis, and subsequently multiple abscesses. What should be done with this finger?

Clinical Clerk: The terminal phalanx should be amputated.

Dr. Niles: Undoubtedly. The only reason that he retains it is because he refuses further surgical procedure, and we are obliged to leave it in this condition, although we realize what a serious menace it is to his well-being. *Staphylococcus aureus* frequently produces osteomyelitis and secondary or pyemic abscesses often follow. I have seen several such cases with Dr. Hartwell this year, and I presented one of them in this clinic last fall. You may recall he was a young man who sustained a crushing injury of his hand and later developed several foci of bone infection; both femurs and one ulna were involved. He eventually recovered after a long residence in the hospital. One other point. Has this patient at any time shown any signs of endocardial involvement?

Clinical Clerk: No.

Dr. Niles: *Staphylococcus aureus* very rarely localizes on heart valves, even in the most severe infection. It is also a rare invader of the meninges. Councilman, in 60 consecutive cases of meningitis, found the following organisms: Meningococcus, 21; pneumococcus, 18; streptococcus, 18; staphylococcus, 2. Bramwell says that the prospect of recovery from an acute purulent leptomeningitis is small, and death is almost invariable in cases with a sudden onset. All observers agree, however, that the chances of recovery are greater in staphylococcal than in streptococcal infection. It is, of course, very doubtful if the antimeningococcic serum administered in this case had any influence upon the course or outcome of the meningeal infection, yet I shall surely inject it in any similar cases that we may have.

The lessons to be learned from the cases we have seen today are:

(1) To at once make a lumbar puncture in every case with any meningeal symptoms.

(2) To at once inject antimeningococcic serum whenever a cloudy fluid is obtained.

(3) To repeat the injections at frequent intervals and in large quantities until the infection is proved not to be of meningococcal origin, or until the patient has recovered.

CLINIC OF DR. ARTHUR L. HOLLAND

CORNELL UNIVERSITY MEDICAL COLLEGE

THE FLUOROSCOPIC METHOD OF DIAGNOSIS IN DIGESTIVE DISEASE

Special Uses. Comparison with Radiography. Limitations. Indications for Combination of Methods. Requisites for Use. Essentials for Equipment. System of Examination. Main Examination (Esophagus. Stomach. Tracing. Peristalsis. Cap and Pyloric Region. Filling Defects. Charting). Second, Third, and Fourth Examinations. Confirmatory Observations. General Remarks. Stereoscopic Fluoroscopy. Illustrated by Photographs Showing Instrument in Vertical and Horizontal Position; Three Types of Cases and Silhouettes of Outlines of Normal and Abnormal Anatomic Findings.

BEFORE proceeding to discuss the fluoroscopic method of diagnosis in digestive diseases I will reverse the usual order of presentation by offering the following summary as an introduction:

The fluoroscope is an instrument of medical diagnosis. It should be used only by those who are actually engaged in clinical medicine and who are experienced or at least familiar with modern laboratory methods. The field for fluoroscopy is a large one; it overlaps that of radiography, but is not a substitute for the latter method.

Special Uses.—The fluoroscope in trained hands will yield information that *x*-ray plates, even in long, expensive series, cannot always disclose. These are: A correct estimation of peristalsis or the presence of a reversed peristalsis; the effect of adhesions on the position, contour, mobility, motility, and rela-

tion of the viscera; the possibility of direct dermatographic charting; the better placing of mass and pressure pain with combined palpation; and the detection and estimation of spasm. *x*-Ray plates in series may suggest these possibilities, but only when interpreted by a master radiologist.

Limitations.—On the other hand, the fluoroscope cannot compete with serial radiography in detecting obscure filling-defects in the cap, pyloric region, and the intestines; the outlining of diseased gall-bladders; the detection of gall- or kidney stones, and accurate mapping out of a diseased area as an aid to the surgeon in determining his mode of procedure. Then, too, the obese patient presents a problem to the fluoroscopist which is not nearly so perplexing when plates are used.

Indications for Both Methods.—When in routine diagnosis the fluoroscopic findings are at variance with clinical and laboratory findings and a diagnosis remains cloudy, supplementary radiography should be employed. Operative cases should be studied by a combination of both methods prior to operation.

Requisites for Use.—Successful fluoroscopy depends in great part on an exhaustive history, a complete physical examination, and all possible aids from the laboratory. It demands a uniform system of procedure, a system which provides for the proper preparation and protection of both observer and patient, and one sufficiently flexible to fit unusual cases. Record blanks and charts are essential. "The Roentgen-Diagnosis of the Diseases of the Alimentary Canal," Carman and Miller (Saunders), will be found a most useful book. "The Alimentary Tract," Barclay (Macmillan), is also helpful and original. These and other works go into mechanical and other details which time will not permit here.

Essentials for Equipment.—I will, however, mention some of the essentials in the equipment. For office use, where a direct current is available, the coil answers every need; in fact, it is for this limited purpose ideal. It is much less expensive in cost and maintenance and, because of its simplicity, easily handled. A standard platinum gas tube of high vacuum is mounted in a suitable stand (Fig. 70). Any one of a dozen makes of stand

can be used. It is essential that the tube box be so constructed that it automatically takes its place directly back of the screen in no matter what position the screen may be placed. At the front of the box a diaphragm should be constructed which can

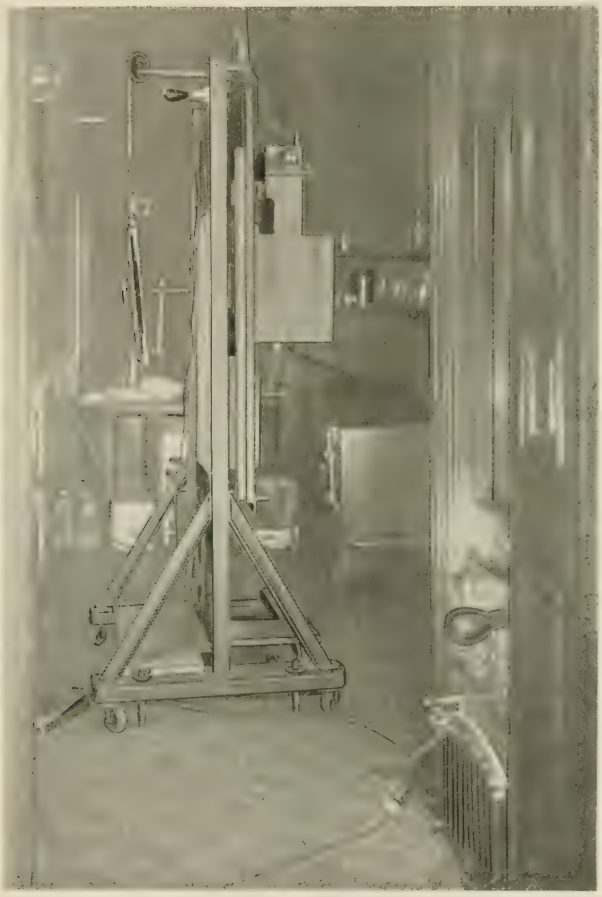


Fig 70 —An antique but practical vertical stand

be regulated by the operator during observations. Some means for cooling the tube should be provided. A miniature electric fan, mounted on the top of the tube box with a window in the box to receive the air, is the simplest arrangement. A foot-

switch is indispensable. A rheostat and either a mechanical or acid interrupter complete the mechanical equipment. Very thorough protection is to be insisted upon in the construction of the stand, and, in addition, the operator should always when making observations wear a leaded rubber apron and heavy gauntlet gloves of the same material. The room should be

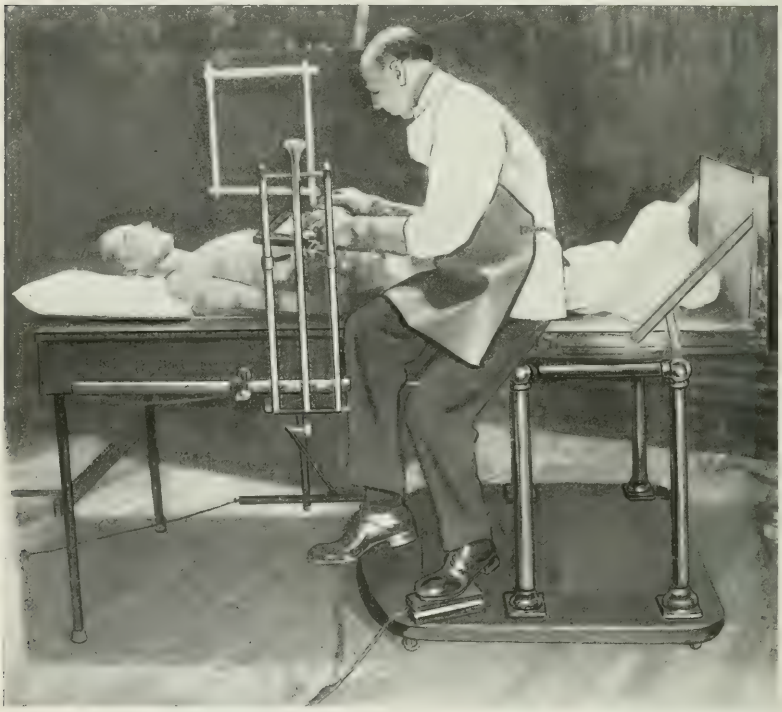


Fig. 71.—A convertible stand being used in the horizontal position (New York Hospital).

capable of being made absolutely dark, but one or two red lights are arranged so that by pulling a conveniently placed string they can be lighted or extinguished.

Where space is valuable, a stand that can be made into a table (Fig. 71) is an advantage, but much time is lost in making this change in position, because of the re-arranging of wires and other mechanical details. A duplicate outfit permanently

maintained, one in the vertical and the other in the horizontal position, is the better plan.

For those who would not be limited to fluoroscopy and who wish to take the instantaneous plates that gastric radiography calls for, a transformer outfit is necessary. The Coolidge tube is convenient in that it can be maintained practically indefinitely at any given penetration, while the gas tube requires frequent regulating.

Each investigator as he progresses in this work will establish a system for himself. His success will be in proportion to his perseverance in carrying out the details of this routine. My own system, built on the work of others and as a result of my personal experience in this field, is as follows:

System of Examination.—At the patient's first visit his history is taken, a complete physical examination is made, and a tentative diagnosis recorded. If a cathartic is not contraindicated, he is ordered to take that night a dose of castor oil and for the three subsequent days he is put on a Schmidt diet. At 10 P. M. of the last day he is required to eat a large dish of boiled rice and milk. The following morning the urine collected from the day before and a specimen of the feces obtained that morning by means of a small enema are sent to the laboratory. The stomach-tube is passed and the stomach contents removed, to be tested for starch and blood. Before the tube is removed a lavage is given. The returned water is saved to be tested for starch and blood. The patient is then given 1 ounce of barium sulphate in $\frac{1}{2}$ glass of water and then is placed on the examining table. His abdomen is thoroughly gone over in a search for mass and areas of pressure pain. When found, these points are marked on the skin with a red wax pencil. This second physical examination of the abdomen is important in order to clear up any uncertain or indefinite findings of the first examination.

The massage and manipulation of the abdomen with the patient in the recumbent position aids the barium to search out and occupy irregularities in the mucosa and to squeeze through the pylorus to help fill out the cap. This extraction and examination is carried out in the dark-room with only the red lights turned

on. A certain amount of time is necessary (ten minutes at least) to prepare the observer's eyes for the screen work.

The patient, stripped to the waist (women are provided with an artist's gown, open at the front), is placed, standing, in front of the fluoroscope stand with his back against the stand and his abdomen against the back of the screen. The tube is now regulated, the observer puts on his protecting apron and gloves. In his right hand he holds a long sponge-holder, into the jaws of which is fitted a short piece of blue dermatograph pencil, capped with a disk of lead. The red lights are now put out by pulling the string. The foot-switch is tested and the aperture in the diaphragm is regulated to give a field of about 8 square inches. The screen is lowered, raised, or moved from side to side until the shadow of the barium is found. The aperture is now reduced to 2 inches and brought to the lowest part of the shadow. A pencil mark on the skin here shows the true position of the greater curvature. As the target of the tube is directly back of the center of the screen, distortion is not possible in charting the exact outline.

Preliminary Observation.—With the aperture still reduced, the entire stomach shadow, including that of the cardiac end, fundus, and pyloric region, is searched for deposits of barium, which may suggest ulcer craters, penetrating ulcer niches, and small filling-defects.

The screen is now raised until the heart shadow is brought to view. The aperture is reduced to 1 inch, and the position of the apex marked on the skin (Fig. 71). Swinging over to the right side of the heart shadow, this is also traced. Raising the screen still higher, two vertical strokes of the pencil on the skin directed by the small aperture, charts the position of the right and left borders of the aortic shadow. The lung shadows are quickly scanned for gross evidence of disease (physical signs and radiography are so much superior to the fluoroscope in lung examinations that too much time should not be used here). After a little experience it will be found that this entire process will not require more than from thirty to forty-five seconds of actual exposure. A skilful use of the foot-switch makes this possible.

The aperture being kept so small most of the time gives not only a brilliant illumination, but also makes it possible to expose any given section of the skin for only a second or two. This preliminary step in the fluoroscopic examination is of the greatest

Fig. 72.—Oblique position for observing esophagus. Convertible stand, vertical position (New York Hospital).

value. It frequently brings to view small lesions that can in no other way be detected, as it enables the barium to filter into spaces that the heavier barium mixture which follows cannot easily fill. Its greatest value to me has been in making it possible to estimate the tonicity of the stomach by comparing the position

of the greater curvature under these conditions and later, when the organ is full of the heavy, opaque meal which follows.

Main Observation.—The lights are now turned on and the patient is rotated somewhat so that his left shoulder rests against the stand (Fig. 72) and his right shoulder against the back of the screen. Into the patient's left hand is placed a glass containing the following mixture:

Six ounces of barium sulphate.
Two teaspoonfuls of malted milk.
Sufficient solution of boiled tapioca to suspend the barium.

This meal should be of the consistency of very thick creamed soup and should measure at least 16 ounces. It should be served hot and should be thoroughly mixed. I use for this purpose an electric soda-water mixer; but an egg-beater will do.

Esophagus.—Before the lights are again extinguished the tube is regulated and the patient is requested to take a few swallows in order to accustom him to the procedure. The room is again darkened and the patient told to continue to drink slowly. With the aperture fully opened, the screen is placed at the level of the chest, where the opaque meal can be observed descending. If this is not clearly seen, the patient should be turned a little one way or the other until it is brought to view, and the aperture then regulated so that there is an illumination of about 3 inches wide running from the top to the bottom of the screen. One soon becomes familiar with the normal fluoroscopic appearance of the esophagus. When it is seen that there are no unusual bulgings and that the meal is entering the stomach without any delay, the observation should be at once shifted to the stomach.

The patient is now placed with his back (Fig. 73) squarely against the stand, but he is told to keep his head turned to the left so that he may continue to drink the mixture. The screen is lowered and the aperture made sufficiently large to take in the entire stomach shadow. The food is seen to enter the stomach from the right side of the magenblase in spurts; it either drops directly to the lowest part of the stomach, or runs down the

right wall until it reaches the bottom, where it spreads, rounding out the greater curvature.

Until the stomach is full there is no need for making observations on the character of the peristalsis. When one is satisfied

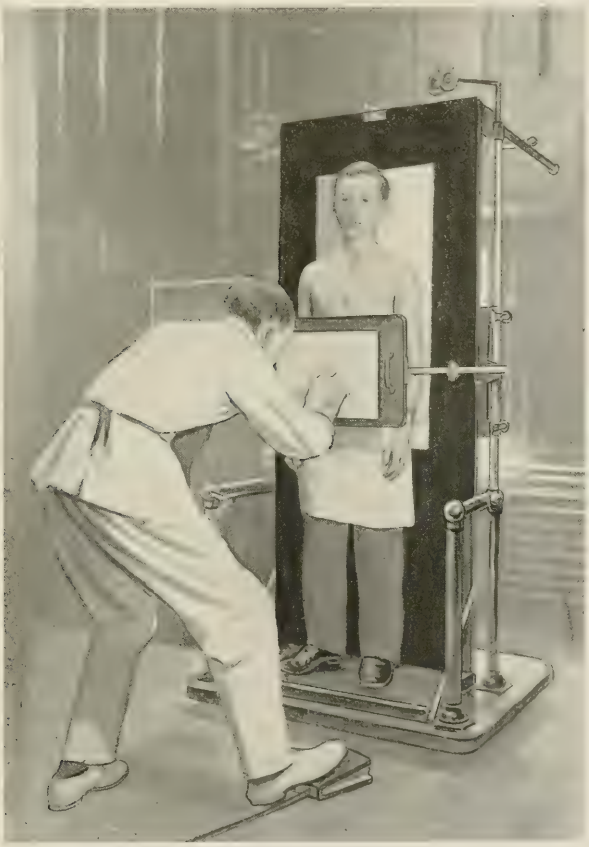


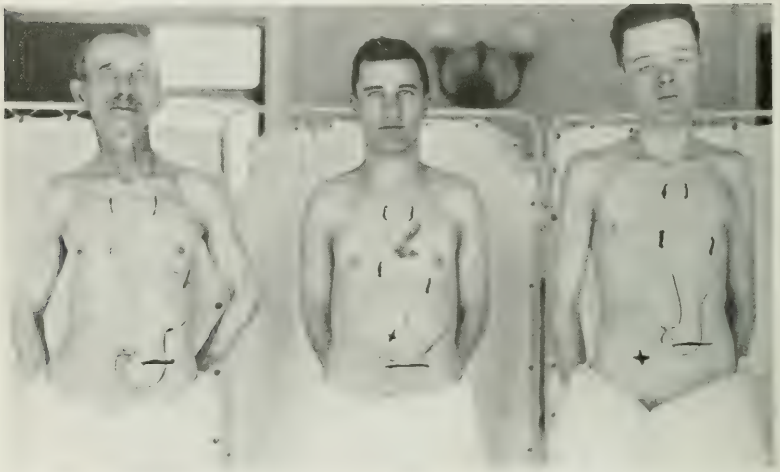
Fig. 73.—Position for observing abdominal shadows (New York Hospital).

as to the mode of entrance and the direction the food takes as it enters the stomach, the observation should be discontinued until all of the meal has been taken. The position of the greater curvature is now marked, using the very small aperture to direct the pencil. The shape of the organ is then quickly determined.

It requires but a second or two to trace the outline on the skin (Fig. 74).

Peristalsis.—Observations on the character of the peristalsis are now in order. One or two minutes will elapse usually before peristalsis begins, but gentle massage will usually start the contractions if they are slow in making their appearance.

A diagnosis of the type of peristalsis is made by counting the waves to be seen at one time along the greater curvature from the



Dull pain. epig. and precor. p. c. and on exertion. Stomach slightly ptosed. Cardiac hypertrophy and a small aneurysm.

Boring pain. epig. two to four hours p. c. and at night. Cap absent. Postpyloric ulcer.

Crampy pain. epig. immed. p. c. Spasm of cap. Ch. appendicitis.

Fig. 74.

fundus to the pylorus and seeing that they are equal with those on the lesser curvature; one wave indicates a one-cycle type, two waves, a two-cycle type, and so on. A wave on each curvature should be watched from its beginning until it stops at the pylorus. It is only in this way that irregularities in contour can be detected.

A false wave or incisure at some point in a wave's progress will be absorbed in the wave and may easily be missed. The

wave will stop at an indurated or otherwise involved area, to begin again beyond, very much as sea waves will smooth out when an island of floating oil is encountered. The niche of a penetrating ulcer with a small induration will ride like a buoy, but if the surrounding induration is extensive the waves will stop as if at a volcanic island, to go on again beyond.

Rugæ, running through and in a direction away from a somewhat irregular contour of one part of the stomach where there also is seen some displacement of the part, are suggestive of adhesions. They are, however, difficult to see without plates. The rugæ or striations that are the result of spasm are more symmetrically placed and are quite obliterated when the spasm is relieved.

Adhesions effectively prevent the regular progress of a peristaltic wave at the point of attachment, and usually for the balance of the distance to the pylorus. The depth to which a wave dips into the surface denotes the strength of the peristalsis. Weak contractions slowly ripple along, making hardly any impression on the contour, while the strong contractions of an active peristalsis will give the appearance to the shadow of three or four balls strung together. There are many degrees between these extremes.

Before shifting the examination to the pyloric region and the cap, which is the most important and most difficult part of the shadow to see and interpret, sustained pressure is made on the lower abdomen to force the opaque meal to fill out the upper part of the stomach so that it can be studied. At the same time this pressure helps to force the opaque chyme through the pylorus and into the cap. In the fluoroscopic shadow the pyloric sphincter is indicated by an interval of about $\frac{1}{4}$ inch, through the center of which runs a stem the thickness of a match-stick, connecting the cap to the ampulla.

Cap and Pyloric Region.—The cap, while arbitrarily described as part of the duodenum (ascending portion), is from a radiologic point of view the terminal portion of the stomach—the "great divide" between its greater and lesser curvatures.

To study the cap and the pyloric portion of the shadow

Fig. 75.—Semidiagrammatic silhouettes illustrating normal and abnormal findings (Cornell Medical College Clinic).

the aperture must be reduced to take in only this region or only a part of it at a time. The contour of the pars pylorica is best seen when sustained pressure is made against the lower abdomen

Fig. 76.—Semidiagrammatic silhouettes illustrating normal and abnormal findings (Cornell Medical College Clinic).

or even higher. The stomach examination is not complete until the patient has been somewhat rotated from right to left and from

left to right. Fluoroscopically, such diagonal shadows are not easily seen, still one can thus occasionally pick up otherwise obscure lesions.

With the proper preparation and a clean stomach well filled with a thoroughly mixed opaque meal of sufficient specific gravity some of the smallest and most obscure lesions can readily be seen. But to do this kind of fluoroscopy one must undertake considerable training. For several seasons at the Cornell Clinic I have in all of our presented cases enjoyed the advantage of having Dr. Cole's serial plates (interpreted by Dr. Cole personally) to check against my fluoroscopic findings, and as many of the patients were later operated upon, have personally seen at the operations what I should have seen, but did not; and have also there not seen what I thought I would see. This kind of training is invaluable to one who does not wish to become narrow from concentrating on one method. The normal shape of the cap and the pyloric region of the stomach should become firmly impressed in one's mind, also the structural departures from the usual forms and functional irregularities which affect the contour or behavior of these parts. To memorize these points one must examine hundreds of normal cases.

It is most difficult to describe the effect of the various lesions on the shadows. This must be learned by personal study in front of the fluoroscope. The use of combined palpation brings out more than half of the points of value about this region, and this can only be demonstrated while actually using the apparatus.

Filling-defects.—Large filling-defects are rarely missed, but one must possess perfect eyesight to pick up the small bites-out-of-the-cap or about the pars pylorica. A re-examination is necessary when such a lesion is suspected, as bits of retained food, local spasm, or pressure from without may be responsible. When not contraindicated, massage of the part and pressure applied below will do a great deal to sustain or discredit such a diagnosis.

By the time the stomach has been gone over throughly in most cases a large portion of the opaque chyme is in the small intestine. If it is seen to accumulate at any one place, indicating

a filling-defect or stricture, that point should be marked on the skin and observed two or six hours later.

Charting.—Before a patient dresses the markings on the skin are examined and the red pencil markings, which are placed to indicate pressure pain, mass, or other physical findings, are compared with the blue tracings. This is all copied at once on the chart and the findings are written or dictated before they are forgotten. I have used in the dark-room a dictaphone for this purpose, but an attendant can just as well do this by dictation.

If possible, the patient should again be seen in two hours. An "absent cap" will at this time frequently make its appearance or, where the peristalsis was at first thought to be absent or excessive, it might now be seen to be quite normal or the reverse.

Second Observation.—A six-hour examination also is necessary to estimate the motility. After this observation the patient is directed to resume his usual diet, except that his breakfast for the following two mornings is to be an Ewald test-meal. The initial dose of castor oil is the only laxative allowed during the course. If, however, the bowels do not empty each day, a small, cold, saline enema is ordered to be taken in the sitting position in the morning.

At this observation (the six-hour examination) all of the opaque chyme should have left the stomach and the head of the shadow should be found in the cecum, or even well along the colon. A flash at this time is all that is necessary, unless one has at the previous examination suspected a lesion. The following morning it is my practice to extract an Ewald test-breakfast before making the colon examination.

Third Examination.—The colon is usually easily seen in its entire length. It is difficult to see the appendix with the patient in the erect position unless the abdomen is palpated and the cecum held up by the operator's left fist, pressed in over the part and held there tightly. Filling-defects and the size, shape, and position of the colon are noted; variations in peristalsis and reverse peristalsis are all watched for through the reduced aperture. Deep palpation will often prove an apparent filling-

defect to be false. Dermatographic charting of the colon is a refinement of considerable value.

Fourth Examination.—An Ewald test-meal and extraction again precedes the observation on the following morning. At this "séance" attention is given to the appendix. If an appendix was visualized on the previous day and is now empty, it is not likely that its motility is impared, but, if still full, the observation should be continued daily until it cannot be seen. Because an appendix cannot be seen at all is not a sufficient reason for a diagnosis of obliterative appendicitis. A retention of over ninety hours is rather suggestive of chronic appendicitis.

Confirmatory Examinations.—When such a series of examinations brings out symptoms radiologically interesting, a special re-examination, directed to the part under suspicion, is in order. For instance, if there was observed any delay or undue bulging of the esophagus at the first examination, a special test should be indulged in, this time using a bread, milk, and barium meal, or, if some irregularities are discovered in the colon, an opaque clysma should be administered and the colon observed with the patient in the horizontal position. A re-examination of the stomach is also in order if there is the slightest question as to the findings in the regular series of observations.

My reasons for adopting and carrying out this routine in all of the cases referred to me are as follows:

One can never be sure that clinical symptoms pointing to an involvement of a given organ are not referred from some distant part. Irregularities observed fluoroscopically at some point might erroneously be made to explain the cause of the trouble, while a distant, unsuspected lesion is really the underlying cause. I combine the physical examination, the laboratory investigations, and the fluoroscopic observations in this manner so that I may obtain a composite picture of what is occurring physiologically or pathologically within a given time. I admit that it seems to be a cumbersome system and it taxes the time and patience of both investigator and patient, but it is necessary for perfect technic.

General Remarks.—In private practice, in order to insure

the regular and prompt attendance of the patient, he is told that he will be expected to give up practically all of his time for one week. The charge is arranged so that one fee covers all the work, no matter how many calls are made or what laboratory tests are necessary. After the first shock this serves to ease his mind and prevents his complaining of the "mounting expense" and it keeps him "on tap."

The reason for prescribing the castor oil in the beginning is obvious. As a gastro-enterologic investigation is incomplete without a fermentation, bacteriologic and microscopic examination of the feces, and as the barium meal would interfere, the Schmidt diet is given before this is administered. The rice motor meal is the simplest test we have for errors in gastric motility. The lavage the following morning serves a double purpose. I have found that twenty-four hours after the barium has been taken the Ewald test-meals give practically the same findings as when they are not so closely associated with the radioscopic preparations.

Those who would do only fine fluoroscopy should never stoop to the time-saving practice of giving the double meal, the first one six hours before the actual examination, when the second meal is given. The resulting shadows in the colon and the many flecks scattered about in the small intestine are not only disconcerting, but in many cases actually prevent a proper visualizing of the stomach or cap. By giving only one meal and watching that as it makes its way through the alimentary tract, one is in a very much better position to judge of the motor equipment, and such information is of great importance in all cases.

Where it seems important to establish the relations between the stomach and some part of the colon a second barium meal may be given after all of the first meal is in the colon, but this is not used in searching for details in the stomach shadow.

I have been criticized for giving so large a quantity of barium as 8 ounces. Thoroughly washed barium sulphate is harmless in double this dose. I have given this meal in more than 1000 cases without one unpleasant incident resulting. I would prefer to discard the fluoroscope rather than to be limited to the 1 or 2

ounces of barium that is usually recommended for this purpose. The dead black silhouette with its clean-cut outlines is not possible with the smaller dose.

Stereoscopic fluoroscopy, the dream of radiologists, has at last been demonstrated scientifically. The manufacturer under whose patronage the experiments have been conducted is prepared to make the apparatus commercially possible as soon as there is a demand for it. That the time is ripe for this innovation there is no question. There is urgent need for it in military surgery for the quick and accurate locating of foreign bodies and in setting fractures. Its possibilities in gastro-enterology and in cardiac, aortic, and sinus diseases are without limit. I am willing to predict that within a few years this method will entirely supersede radiography.

CLINIC OF DR. H. RAWLE GEYELIN

PRESBYTERIAN HOSPITAL

SYMPOSIUM ON DIABETES

DR. GEYELIN: It is appropriate at this time when you have finished your fourth year in medicine to summarize in certain disease which have been studied intensively by various groups of students during the past year. Today we propose to present to you certain phases in the diagnosis and treatment of diabetes. The students who have followed these cases in the wards under constant supervision will summarize some of the most interesting results obtained. I will ask Mr. Hyman to discuss briefly the experimental facts upon which the modern treatment of diabetes is founded and then present to you a brief summary of the treatment itself.

MR. HYMAN: Some of the knowledge upon which we have hitherto based our treatment of diabetes has been derived from experimental facts, but a large part has been based upon theory. Fortunately for the diabetic patients Dr. Allen has within the past five years advanced a very successful method of treatment based on elaborate and well-planned experimental study of diabetes in animals, and confirmed by work on a series of 70 or more diabetic patients.

A brief consideration of these experimental results and their application to human diabetes is a necessary preface to any discussion of diabetes. Dr. Allen believed that diabetes was the result of weakness of pancreatic function. In order to imitate this weakness experimentally he removed varying portions of the pancreas in dogs, leaving, roughly, a remnant of a twelfth or an eighth of the gland. Those dogs with the larger remnant of pancreas comparable to our milder cases of diabetes showed few

symptoms unless overfed, and responded quickly to withdrawal of food in appropriate amounts. Those with the smaller fragments of pancreas left *in situ* comparable to the severer diabetes as seen in young people, developed symptoms on feeding which were less amenable to withdrawal of food, and if food was continued death invariably resulted.

The milder type may be converted into the severe type by giving sufficient food to maintain glycosuria, the subsequent course of the disease being in every way comparable to that observed in severe diabetes in man. Allen has also been successful in producing the symptoms of acidosis in these dogs, a feature of the analogy of experimental to human diabetes which has hitherto been wanting.

To explain the disturbance in carbohydrate metabolism produced by these experimental procedures Allen advances the theory of deficiency of pancreatic amboceptor which under normal conditions acts as a bond between sugar and tissue, rendering the sugar susceptible of oxidation. As a result of this deficiency of amboceptor the body loses its ability to utilize COH, and sugar is lost in the urine. To supply this deficiency in COH the organism calls upon the body protein and fat—58 per cent. of the protein molecule being capable of transformation into sugar—this portion of the protein molecule in part helps to make up for the deficiency in COH, but in the absence of sufficient amounts of COH the normal fat metabolism is perverted and toxic intermediary products of fat metabolism are produced, these in turn being chiefly responsible for the ensuing acidosis. Acidosis in itself exerts a certain influence in producing hyperglycemia and glycosuria, and so the vicious cycle is complete.

With these prefacing statements on the experimental and theoretic aspect of diabetes we come to the more practical consideration of actual treatment.

The Fast.—The main effect of fasting is to abolish glycosuria and diminish the blood-sugar. There is another important effect produced, and that is the abolition of acidosis. There are very few cases who do not respond to this method of treatment, and in these cases the acidosis may be intensified by the initial fast.

It is in these same cases, as a rule, that fasting also fails to clear up the glycosuria, but after a period of low feeding, preferably protein, both the acidosis and the glycosuria usually disappear on a second fast; rarely a third fast is necessary. Former authors had always believed that withdrawal of food increased acidosis, but with very few exceptions they did not have the courage to prolong the fast.

The effect of the fast to diminish protein metabolism is, in reality, nothing but a part of the effect of the fast in decreasing total metabolism, the latter being lowered by fasting or at least by fasting plus subsequent low feeding. The decrease of the total metabolism, in turn, means a lowering of functional need in general, with its consequent rest of the overtaxed pancreatic function.

As regards the beneficial effects of fasting on the metabolism of fat, the question is not so clear. This much is probable: thin people whose fat supply is meager because they have not much fat to draw upon, do not form the perverted intermediary products of fat metabolism, acetone, diacetic acid, and oxybutyric acid to the same degree as do fat people; therefore, thin people as compared to fat people are more apt to diminish the acidosis as a result of the fast. With very obese people, on the other hand, sudden institution of the fast increases the production of the acid bodies, and unless elimination is adequate the resulting acidosis is often extreme and the sudden introduction of complete fast in these people is, therefore, dangerous. The danger of fasting obese individuals has been emphasized by Folin in the case of normal people.

Of course, in both thin and obese individuals the lowering of total metabolism produced by the fast must have its effect in diminishing what would otherwise be a more rapid catabolism of fat.

The effect of fasting upon body weight and fluid exchange will be dealt with later in this discussion and need not be referred to here.

The After-fasting Treatment.—It must be remembered that the most important function of the fast is to eliminate glycosuria

and acidosis, but its effect in increasing future food tolerance is one that cannot be overlooked. That this tolerance is increased in most cases has been amply shown, and it is with this in mind that intermittent fast days even in the absence of glycosuria are advised during the subsequent treatment.

After rendering the patient sugar free, our next step is to start feeding, preferably carbohydrate. This is gradually increased, in amounts from 5 to 10 grams daily or on every second day, adding sufficient fat and protein to make the diet palatable and further to meet caloric loss, but keeping the total amounts of these substances low until the sugar again appears. This is eliminated by another fast day and the carbohydrate limit just attained is cut in half or even lower, while fat and protein are added gradually to the diet up to the point of tolerance. After an intervening fast it may be advisable to increase gradually the COH, maintaining the COH, protein, and fat at a level below that of actual glycosuria. At this point the total food intake may be kept constant depending upon the circumstances surrounding the individual case. It must be emphasized here that it is never desirable to increase the fat simply for the purpose of increasing the total calories. The patient should be taught to live at that level of metabolism which will keep sugar from the urine and prevent acidosis, the degree of activity being regulated by the total calories received and not by the former activity of the patient, an occasional fast day or half-day being interposed at regular intervals with the hope of increasing tolerance. I have tried to present in brief form the principles upon which this universally adopted method of treatment is founded and more briefly the general outline of actual treatment.

Mr. von Hoff: The chart shown on the board is a graphic illustration of the course of diabetes in a young woman, A. P., aged nineteen, whose chief symptom on admission to the hospital was polyuria. The duration of this symptom was six weeks. Except for slight loss of weight and a history of irregular menstruation, epigastric discomfort, and failing memory, there were no other symptoms. The physical findings were negative except for large broad hands and feet and enlarged thyroid. The patient

was fasted immediately and after six successive fast days became sugar free; during this time the ketonuria diminished and the blood CO_2 rose. There was definite retention of fluid and slight loss of weight. Carbohydrate was fed in gradually increasing amounts (10 grams daily) until 100 grams were reached (protein and fat intake being kept very low); at this point glycosuria appeared. The weight had been steadily decreasing, and after a second fast day the carbohydrate was halved and protein and fat gradually added until the total food amounted to 1500 calories. At this point sugar reappeared. A fast was given and this eliminated the glycosuria. From this time on until discharge the diet, varying from 1000 to 1400 calories, was given without the reappearance of sugar, one fast day having been interposed in the meantime. Total loss of weight during the stay in the hospital was 20 pounds.

Mr. Kohn: The influence of fat feeding on glycosuria and acidosis. Under former methods of treatment the withdrawal of carbohydrate from the diet was followed by substitution of large amounts of fat. That this was harmful to the patient's tolerance has been amply demonstrated by the work of Allen. But what is equally important is the effect that this continued high fat feeding had on increasing acidosis.

The case illustrated by this chart will emphasize these points. Here is a patient whose carbohyrate and protein were kept at a comparatively low level, 30 gm. COH and 60 gm. protein, while the fat was maintained at 150 to 200 gm. for three weeks. You will see that although the patient was sugar free all this time (with one exception) the blood-sugar steadily rose, the blood CO_2 slowly decreased, and moderate amounts of diacetic acid persisted in the urine. Finally, we have sugar appearing in the urine which required two fast days to clear up. Fat is now diminished to 60 gm., while the carbohydrate is more than doubled. In spite of this increase in COH, we see a drop in the blood-sugar, the urine remains sugar free, blood CO_2 rises, and the ketone bodies gradually disappear from the urine. The loss of weight amounting to 6 pounds in two weeks is seen. Finally the fat and protein during the last week of the patient's stay in

the hospital were increased to 90 gm. each, while the COH remained the same. The patient was then discharged with a blood-sugar of 1.8 gm. per liter, a normal blood CO_2, and without ketonuria; weight was not regained.

In concluding I wish to emphasize one point, and that is the unreliability of acetone and diacetic acid in the urine as an index of acidosis. The chart of this case illustrates this point. We have here a patient who showed a persistent and quite marked ketonuria subsequent to his becoming sugar free, this in spite of the fact that his alveolar and blood CO_2 were normal and his general condition was that of well-being without any signs of acidosis. It was only on long-continued underfeeding with fast days that the ketonuria finally disappeared. Formerly this would have been regarded as a dangerous sign, but with the added aid of modern work on acidemia we are enabled to exclude ketonuria *per se* without other evidence of acidosis as a danger sign, provided that the blood-sugar remains low and that the patient is free from glycosuria.

Mr. Solovei: Comparison of results observed in the young diabetics of severe type who yield readily to treatment with less severe cases of the same age whose onset has been more gradual and who yield less readily to treatment. The acute cases of diabetes I will designate as Type I and the cases of longer standing Type II.

Manner of onset in:

Type I.—Case 1 : C. K., male, age nineteen. This patient first noticed symptoms six weeks before admission to the hospital in a precomatose condition.

Case 2: L. W., male, age seventeen. Came into the hospital in a similar condition. Had first noticed symptoms three weeks previously.

In both these cases the symptoms noted were those of typical diabetes in its most severe form, loss of weight in each case being extreme.

Type II.—Case 1: E. F., female, age sixteen. Onset was more gradual, lasting over one year before admission to hospital. Aggravation of pruritis vulvæ led to examination of urine.

Although patient had lost much weight there was only slight acidosis and no signs of coma.

Case 2: L. D., female, age twenty-eight. Onset also gradual, lasting thirteen months. Loss of weight moderate, 25 pounds from time of onset to admission to hospital. Also in this case there were no symptoms to suggest coma and only mild acidosis.

Loss of weight:

Type I.—Case 1: C. K., lost 40 pounds in six weeks, or an average daily loss of 1.1 pounds.

Case 2: L. W., lost 30 pounds in twenty-one days, or an average daily loss of 1.4 pounds.

These two cases from onset to time of lowest weight lost 24 and 28 per cent. respectively.

Type II.—Case 1: E. F., lost 22 pounds in nine months, an average daily loss of 0.08 pound. Percentage loss of original body weight being 18 per cent.

Case 2: L. D., lost 25 pounds in thirteen months, or an average daily loss of 0.064 pound. Percentage loss of original body weight being 20 per cent.

Glycosuria on Admission.—Type I.—Case 1: C. K., excreted 75 gm. sugar daily on first three days of admission, which were fast days, and it required twenty-two days for this patient to become sugar free. From time of admission to time of lowest weight he lost 26 additional pounds.

Case 2: L. W., excreted 77 gm. sugar daily on first three days and it required fifteen fast days for this patient to become sugar free. He lost an additional 11 pounds during treatment.

Type II.—Case 1: E. F., excreted 13 to 1 gm. sugar daily on first four days and then became sugar free. Her tolerance was about 600 calories for many months and only once for a short time reached 1300 calories. When the tolerance was about 1000 calories 50 gm. COH was being given.

Case 2: L. D., excreted a small amount of sugar on first fast day and then became sugar free.

Acidosis.—With Type I the acidosis in both cases was of the most extreme type not only as regards blood and alveolar CO_2 but also as regards amounts of ketone bodies.

With both cases of Type II the acidosis was only moderate or slight, but was persistent.

Subsequent Tolerance.—Here the differences between the two types was most striking. In Type I, Case 1, the tolerance for COH was 250 gm. forty-five days after he became sugar free, and eight days later it was 170 COH, 120 protein, 200 fat, fifty-three days after he originally became sugar free. With Case 2 the tolerance was considerably above 80–20–2 when he was sugar free, but on the day that he showed only a faint trace of sugar he had stolen considerable amounts of food estimated at twice his allowed dietary.

Type II: Both these cases had persistently low tolerance, never exceeding 50 COH, 20 protein, 2 fat in Case 1, while with Case 2 the tolerance in spite of repeated fast days never exceeded 40 gm. COH, 20 protein, 2 fat, or another diet with COH absent and 500 calories made up of protein and fat, and it finally became impossible to keep her sugar free .

The **blood-sugars** in these cases are also of interest. In Type I, while the blood-sugar was high in both cases on admission, it rapidly sank to normal level, as instanced by Case 1, whose blood-sugar on admission was 3.2 gm. per liter, and one month later it was 0.9 gm. per liter and remained low until discharge. The same holds for Case 2, whose blood-sugar fell from 3.1 to 1.2. In Type II, however, blood-sugar on admission was for Case 1, 2.28; for Case 2, 2.86, and at no time within the next two months did the blood-sugar sink below 1.7 for Case 1 and 1.96 for Case 2.

Mr. Backwin: *Demonstration of Actual Diets.*—Here we have the various food-stuffs eaten by the patient during the twenty-four hours. This dietary, as you see, is divided into three meals and consists of—Breakfast: Tomatoes, eggs, coffee, and one small piece of bread, a small amount of cream. Lunch: Chicken, white of egg, beans, and asparagus. Dinner: Lean round steak, cabbage, and tomatoes. The total food intake amounting to 30 gm. COH, 40 protein, and 30 fat. This is a low caloric diet.

In this table the food for the day is divided into three meals

in a diet amounting to COH 100, protein 100, fat 100. You will observe that in this diet, in addition to the usual 5 per cent. vegetables, it is possible to add foods of much higher percentage COH, such as cereals: 70 per cent. COH, bread 50 per cent. COH, and potatoes 20 per cent. COH. Also that there is considerable meat, eggs, and cheese, and of the fats there is butter and cream. This diet for a diebetic is a high caloric diet and indicates a good tolerance.

All the foods given are weighed uncooked and served to patients in their entirety, none of the materials being left in the vessel in which they were cooked. There are a few exceptions, one being bacon, when it is impossible to serve all the fat left in the vessel in which the bacon was cooked. Salt is added to these diets in weighed amounts and liquids are allowed *ad libitum* in most uncomplicated cases. Coffee, tea, and thin soups are not accredited with any food value.

Mr. Hayes: The following table is presented in order to demonstrate the results obtained in the treatment of diabetes mellitus when the older methods of treatment were employed as contrasted with the results obtained since the general adoption of the Allen principles of treatment. The figures which are found in this table comprise all of the cases which have been treated in the wards of this hospital during the past four years:

		Total cases.	Deaths. Total.	Deaths. Per cent.	Coma.	Coma. Per cent.	Discharged sugar free. Total.	Discharged sugar free. Per cent.	Discharged ketone free. Total.	Discharged ketone free. Per cent.
Former treatment	1913	19	3	16.3	1	33.3	11	62.7	3	16.3
	1914	21	4	19.1	3	75	6	33	4	19.1
Allen treatment	1915	17	1	5.8	0	0	15	88.2	13	76.4
	1916	58	5	8.6	2	40	46	79.3	42	72.4

It is an interesting point of comparison that the number discharged sugar free under the old treatment in 1913 was only 62.7 per cent.; in 1914 only 33.3 per cent. During the first year of Allen treatment 88.2 per cent. were discharged sugar free, while in the second year 79.3 per cent. In the first year, 1913, old treatment, those discharged ketone free were only 16.3 per cent; 1914, ketone free 19.1 per cent.; first year of Allen treatment,

ketone free 78.4 per cent.; last year 72.4 per cent. The total number of cases for 1913–14 is 40, of those 7 died, a percentage mortality of 17. The total number of cases in 1915–16 is 75; of these 6 died, a mortality of 8 per cent.

Thus we see that the modern methods of treatment have reduced the mortality from all causes to a little less than half. Joslin in a much larger series of cases places the mortality at 28 per cent. under the older method of treatment and 11 per cent. under the newer methods.

Mr. Ill: I wish to discuss briefly the occurrence of edema. By edema in diabetes we do not mean edema which is associated with accompanying conditions like nephritis, but that which occurs during the fasting period or subsequently, in uncomplicated cases. Of the cases in this hospital it has been noticed that edema comes on during the fasting period. During the beginning of the fast in these cases one usually finds loss of weight; we also find that elimination of fluid is greater than intake of fluids. After a day or so fluids are retained and the weight goes up. This is particularly true if salt or carbonate is given. The retention of fluids in the absence of sodium carbonate is very likely brought about by salts which are taken in with thrice-cooked vegetables and sodium chlorid which is added to make them palatable. How this acts cannot be taken up here, as it involves the whole subject of edema about which much is still unknown, but salts apparently get into the tissues and thus cause retention of fluids. The edema does not materially differ from the edema which is found in any other condition. It is usually seen over the tibiæ and spreads in a manner similar to other edemas. It has been an interesting fact that in a few cases noted in the hospital patients may gain as much as 8 or 9 pounds in weight without showing any physical signs of edema, pitting, etc. In diabetes, edema is apparently a compensatory phenomenon, as during the fast period and with onset of edema there is marked decrease in acidosis, and the blood CO_2, which in the beginning of the fast period is low in many cases, 14 or 15 in terms of alveolar air, goes up during the fasting period to normal or a little below normal. The edema retains sodium and potassium salts in the

blood. These bases, which are combined with weakly acid substances, have their weak acids replaced by stronger acids, neutralizing them and setting free the weaker acids, which are more readily removed by the lungs and kidneys. The edema probably aids in maintaining the normal acid base equilibrium.

DR. PETERS: Effect of feeding on acidosis. When I speak of acidosis I refer solely to a condition of decreased alkalinity of the blood, and this condition may or may not be accompanied by ketonuria. In the light of our present knowledge it is no longer correct to speak of ketonuria or acetonuria as acidosis. Older text-books have led us to believe that the terms were synonymous, but it is now a well-established fact that acidosis may exist without ketonuria. To put it in still another way, acids other than oxybutyric acid and its derivatives are found at times to be responsible for a lowered alkalinity of the blood. We have considerable evidence that all cases of acidosis are not entirely due to faulty metabolism of food, and we also have evidence that all the symptoms which are commonly associated with ketonuria and ketonemia are not due to diminished alkalinity of the blood.

However, what I wish to discuss are the actual changes in blood reaction, its diminished alkalinity in certain cases of diabetes, the restoration of the normal reaction by means of fasting, and finally, the relation of feeding to acidosis.

This is the graphic chart of a very severe case of diabetes with marked acidosis both in the older and newer sense. This type of case reacts best to fasting, at least as far as acidosis is concerned. This case with several others treated in this hospital in the past two years was cleared of acidosis during the fast. Whether these cases would have responded the same way under the administration of sodium bicarbonate we do not know. We do know that in none of these severe cases treated by starvation alone has the acidosis failed to diminish. We have seen one case whose acidosis on admission was already severe. He increased this acidosis while fasting and taking large amounts of sodium bicarbonate. This patient had a blood CO_2 of 30 on admission, and at the end of three fast days accompanied by large amounts of sodium bicarbonate, the blood CO_2 fell to 20. Of course, this might also have happened without the use of car-

bonate, but in view of the results obtained with the other severe cases without carbonate we believe that in this particular type of case the best results are obtained on fasting alone. The dangers of fasting in acidosis have been much exaggerated, especially in the severe diabetics, the type that we have formerly considered the most dangerous to fast.

The situation as regards the effect of feeding on acidosis is still in somewhat of a quandary. In general, we have found that the titratable acids in the urine run parallel with the blood CO_2, and also, except for a few very peculiar discrepancies, parallel with the alveolar CO_2. Of course, the methods employed in these determinations vary in sensitivity.

Now after feeding the ordinary mixed diet to a normal individual there is very little change in the blood CO_2. When carbohydrate alone is given to a diabetic we have observed a diminution in acidosis (blood CO_2 rises), and, as a rule, a diminution in the titratable acids of the urine. We have also found that as we increase the food intake after the fast in a diabetic individual, if the diet be a mixed one, the acid excretion is increased. As this diet increases there is a further increase in acid excretion. There have been certain exceptions to the above statements and the significance of these results is not entirely clear. That there is considerable interdependence between acidosis and glycosuria cannot be doubted. What this relation is is not entirely clear, but we have found that in all our severe cases the acidosis has always cleared up before the total disappearance of glycosuria, and it is well known that by increasing the acidity of the blood hyperglycemia results.

After the fast we have seen that carbohydrate feeding diminished the acid excretion in the urine. While in a few instances protein feeding increased acid excretion or at least failed to diminish it, these results are not clear cut and no conclusions contraindicating protein feeding have been drawn.

Certain other evidence in connection with the above results are of interest. We have tried the effect of feeding sodium carbonate upon the total food tolerance, and in 2 cases at least there has been a definite increase in the tolerance. When considerable glycosuria was present we have succeeded in greatly

diminishing this glycosuria, food intake being constant, by the administration of sufficient carbonate to make the urine alkaline. These results confirm certain findings of Underhill and others relative to this subject.

DR. GEYELIN: In concluding today's symposium I wish to discuss briefly the treatment of cases of diabetes subsequent to the determination of total food tolerance. This determination of total food tolerance is usually made while the patients are still in the hospital, and it is then that they are taught, as far as possible, to calculate their own diets and test their own urine for sugar. Having determined the total food tolerance, the earlier method employed in this clinic was to keep the patient on a diet slightly below his tolerance with instructions to fast once weekly or once every two weeks, depending upon the severity of the case. Of course, in case of glycosuria an additional fast day was ordered with subsequent reduction of the diet. If patients remained sugar free for one to three weeks on this treatment, a slight increase in carbohydrate was allowed, such as 10 grams per week, always insisting upon a regular routine fast day. We have lately adopted a somewhat different routine, the principle upon which this routine depends is: "an even distribution of the regular fast days throughout the regular food days." This may be more clearly defined by giving a comparative illustration of the two methods of treatment. Under the former routine we will say that a patient's tolerance has been established at 1200 calories per day, that is, on this caloric intake he is just free from sugar in the urine, but if we gave him as much as 50 additional calories, sugar would appear in the urine. On this total caloric intake of 1200 the patient would receive two fast days in fourteen days. His total caloric intake for these fourteen days would, therefore, be 1200×12, or 14,400 (subtracting 2400 calories for the two fast days given). Now let us assume that instead of giving that patient his full 1200 calories per day, we reduce his daily intake to 900 calories or three-fourths of his total tolerance. At the end of two weeks without fast days he will have received 12,600 calories, which is 1800 calories less than he would have received under the other method of treatment. Theoretically this should have the same effect as three and a half fast days in

resting pancreatic function and for the two weeks' period as compared with the older routine method gives one and a half more days of fast.

Practically it has been noted that the results obtained by this last form of treatment are equally good in certain cases as when weekly fast days are given. We have also employed one-half food days as a substitute for fast days, four being given in a two-week period. The results seem to be equally good. In certain cases satisfactory results have been obtained with each one of the above-described methods of treatment. The method of treatment to be employed in any given case can be determined only by circumstances surrounding that case. For instance, if patients do not object to fasting, if it gives them no discomfort, regular fast days are still given, while the food days are reduced somewhat (nine-tenths) perhaps of the total tolerance. In other cases when the fast days are found to be very objectionable the patients are given a lower caloric intake, as in the second method described, without regular fast days. It must be remembered, however, that whatever the theoretic advantages may be in distributing the fast, as described above in Method 2, there are certain cases who seem to do better—*i. e.*, maintain or increase their tolerance—only when the complete fast day is used routinely. This applies more particularly to those cases of low and rather fixed tolerance.

In judging the effect of any treatment for diabetes it must also be kept in mind that there are great weekly and even daily variations in the tolerance of many patients. Also that there are great individual variations in tolerance depending upon what form of food is fed, certain given caloric intakes being better borne when fat is reduced and COH and protein increased in amounts necessary to keep the total calories at the given level. All these variations serve to emphasize the complex nature of this disease, but many of the former complexities have been dissipated by the Allen principles of therapy, which have two great advantages over any previous form of treatment. These advantages are: first, a rational therapy based upon experimental facts; second, in the vast majority of cases much better results are obtained from the standpoint of the patients and a longer prospect of life is offered.

CLINIC OF DR. JAMES J. KING

HOSPITAL FOR RUPTURED AND CRIPPLED, NEW YORK CITY

SYSTEMIC CONDITIONS AS THE RESULT OF TONSILLAR INFECTIONS

I. Acute Endocarditis, Valvular Disease Complicated by Pericarditis with Effusion.[1]

II. Chronic Infectious Arthritis.[2]

ACUTE ENDOCARDITIS, VALVULAR DISEASE COMPLICATED BY PERICARDITIS WITH EFFUSION

THE first patient, J. S., aged twenty-seven, whose history I will relate, was admitted to the hospital on March 23, 1917, with a complaint of pain in the chest, abdomen, and legs from which he had suffered for five days.

Family history was good; parents living and well; one brother and one sister living and well. He is married and his wife and two children are living and well. No history of chronic or infectious disease in his family.

Previous History.—Has taken alcohol in moderation. Does not use tobacco. Appetite good. Bowels regular. During childhood he had frequent attacks of sore throat. At twelve years of age he had similar attacks of pain in knees, ankles, and heart, and again three years ago. Denies venereal disease.

Present Illness.—Began five days ago with pains in the joints and heart, the condition gradually growing worse, progressively involving joint after joint.

[1] This is a case that has apparently been cured, though there is a possibility of recurrence, as the tonsils, the source of infection, have not been removed.

[2] This is a case in which the focus of infection has been discovered to be in the tonsils. Now under treatment.

Examination on admission revealed the following: Temperature 104° F., pulse 90, respiration 24. His general appearance was that of a poorly developed young man. He was dyspneic, with cyanosis of lips and pallor of face. He had all the signs of being acutely ill. Eyes and ears were negative. His tongue was tremulous and covered with a thick, scaly, brownish coat. Lungs showed poor resonance, vesicular breathing throughout. No adventitious sounds. Abdomen negative. Joints of both knees and ankles tender, showing limitation of motion, with pain. Extremities cyanosed. Pharynx slightly congested. Tonsils congested and painful. Heart: Heaving impulse seen and felt over precordium. No thrills in recumbent position. Apex 4½ cm. outside of left nipple line. Right border 5 cm. to the right of sternal border. Sounds barely heard, of poor force and quality, followed by a systolic blowing, soft murmur. Pulses dicrotic, suggestive of Corrigan.

Summary of Examination on Admission.—Hypertrophied heart, mitral regurgitation, painful joints, cyanosis of lips and extremities, dicrotic pulse, inflamed tonsils, septic temperature.

March 26th: Numerous petechial spots over the hard palate and very much reddened tonsils.

April 4th: Right-sided tonsillitis; left border of heart 14½ cm. from midsternal line in fifth interspace; visible pulsation of peripheral vessels, pistol-shot sound in femoral; capillary pulse in fingers; systolic murmurs at apex with short diastolic. Over the second right costal cartilage there is a rough systolic murmur transmitted into the vessels of the neck; no diastolic murmur heard here.

April 7th: Systolic murmur heard over aortic cartilage, transmitted into vessels of the neck and outward along subclavian. Pulsus bisferiens; aortic stenosis and insufficiency.

April 12th: The outline of cardiac dulness at level of fifth rib 8 cm. to right of median line and 9 cm. to left of median line. The chest was aspirated in seventh, eighth, and ninth spaces in postaxillary line. Beady fluid obtained in eighth interspace. There was apparently no space between the lung and chest wall.

April 13th: Fifth intercostal space tender, and over the tender

area a to-and-fro friction-rub may be heard. The left base is very dull, but the axilla is resonant. No pupillary changes. Pulsus paradoxus not obtainable on account of the prostration of the patient. Pericardial effusion.

April 14th: The friction-rub is heard today over a larger area.

April 15th: Pericardium aspirated by Dr. Sellenings in fifth space close to sternum on left side; also from below xiphoid and at cardiohepatic angle. Left pleura aspirated just below left scapula; no fluid obtained. Patient apathetic all day.

April 16th: The left border of the heart is 13 cm. from mid-sternum in fifth interspace. The right border is 5 cm. in fourth interspace. The friction-rub is heard today in the second interspace. The heart action is more rapid, about 94, and there is a typical Corrigan pulse—occasional auricular. Extrasystole audible at apex. The left chest posteriorly is dull from mid-interscapular region to base. Some dulness at extreme of left base. No auscultation phenomena can be obtained owing to the patient's condition (shallow breathing and prostration). No edema of feet.

This man has a history of troublesome tonsillitis and rheumatism during his past life. The tonsils caused him almost constant trouble during childhood. On March 23d he was admitted to Gouverneur Hospital, with acute endocarditis and arthritis. He was running a septic temperature and was a very sick man. His heart was enormously enlarged and in a bad state of decompensation. The *x*-ray photograph of the heart is very interesting (Fig. 77).

Under the regular hospital medical and surgical treatment he rapidly became worse. About April 20th Dr. Camac, the medical attendant, asked me to examine the patient for a focus of infection. He was then unable to lie down, and it appeared to all of us who saw him that he might die at any time. When Dr. Camac asked me to see him he said, "I think we will have an autopsy on him before long."

All routine laboratory work had been done upon him, such as Wassermann, urinalysis, blood counts, blood-cultures, etc.

The Wassermann reaction was negative and so was the blood-culture.

A culture was made from the crypts of his tonsils. An almost pure growth of Staphylococcus albus developed on the plate

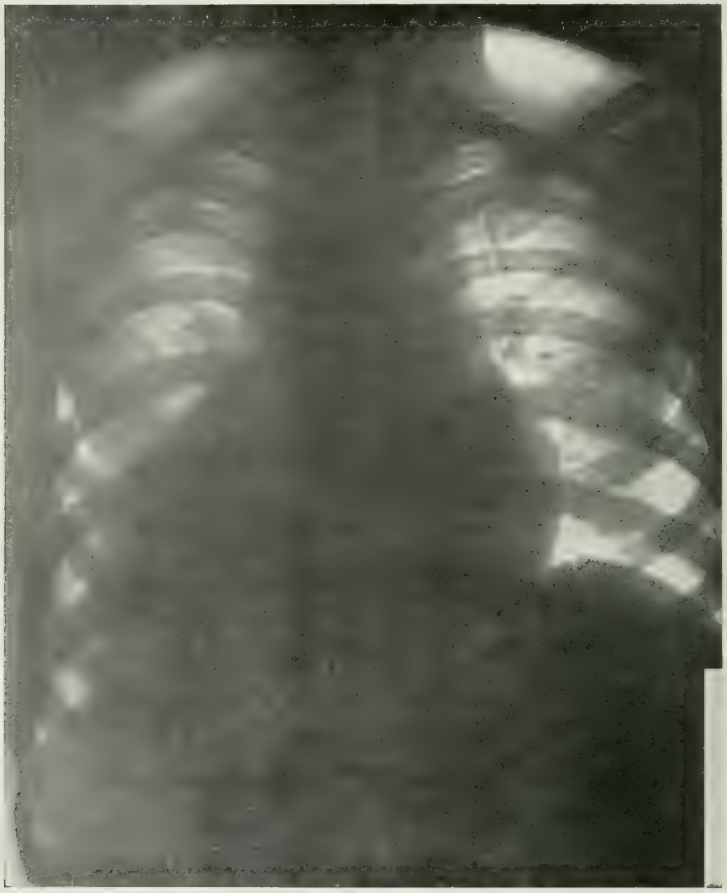


Fig. 77.—*x*-Ray of heart of patient on admission.

within twenty-four hours. An autogenous vaccine was prepared for him, and he was given 100,000,000 by hypodermic injection on April 26th. The injections of the autogenous vaccine were continued every second day and the dosage gradually increased to 300,000,000. Much to the surprise of all of us who had seen

him, his improvement was rapid and continuous, until he felt so well that he refused to stay longer in the hospital. His temperature became normal, his heart action better, and the *x*-ray plate taken before he left the hospital shows a very different

Fig. 78.—*x*-Ray of heart in Case I taken ten days after the first injection of vaccine.

picture from the one two weeks before. The last radiograph shows an enlarged heart, but much smaller than the one taken ten days previously (Fig. 78).

The notes on his chart for April 27th are as follows: No cardiac embarrassment, temperature generally lower. No fric-

tion-rub is heard. Less effusion in the past few days. No cardiac decompensation, less dulness, and clearer breath sounds.

April 30th: Pericardial effusion is being absorbed. Area of cardiac dulness very much smaller. No friction. No cardiac decompensation.

This patient left the Gouverneur Hospital May 20th. His general condition, as well as his cardiac condition, was greatly improved. All of us who saw him when he was so desperately ill marvelled at his recovery. Our opinion was that the tonsils should be enucleated, but he would not consent to the operation. He felt so well that he was content with his improvement.

We might add a word, in general, on the treatment of such patients. We found the focus of his infection in his tonsils—the Staphylococcus albus—and the autogenous vaccines apparently cleared his condition up very rapidly. It is difficult to absolutely prove medical facts, but it appears that the vaccines saved the man's life. He was gradually getting worse under ordinary treatment—digitalis, sodii salicylate, bicarbonate of soda, etc.—but as soon as he received vaccines his improvement began.

We who have seen a considerable number of such recoveries are therefore convinced that the vaccines are efficient in suitable cases. We have encountered some opposition, both by physicians and patients, to the removal of tonsils in patients with cardiac lesions. It has been our privilege to operate upon a score or more of patients with various cardiac lesions, and, without exception, such patients have stood the operation well, and usually the heart lesion has improved after the tonsils were removed. The patients mentioned were operated upon because it was believed that the focus was in the tonsil. The question of tonsillectomy for such patients should be, therefore, carefully considered. The question of anesthesia in these patients should also be carefully weighed. We have operated upon some under ether and others under local anesthesia, considering carefully what is best for the particular individual. It seems to us that just as a focus of infection is searched for in arthritis, so also should a focus of infection be assiduously looked for in lesions of the heart, such as

myocarditis, endocarditis, etc. We have frequently seen cardiac murmurs disappear and the heart become normal in function after the focus of infection has been removed.

CHRONIC INFECTIOUS ARTHRITIS

The first patient to be presented before you today represents a common type, and such cases are frequently seen by all practitioners, whether they are surgeons, general practitioners, or specialists of the most limited type. She has been afflicted for about ten years with a condition which was formerly, although erroneously, called "rheumatism." Her case is typical in every respect, as are several others also to be shown today.

She is a well-nourished young woman, thirty-five years of age. Her history previous to 1906 is unimportant so far as her present condition is concerned, and we pass over it. In 1906 or 1907 she had a severe tonsillitis which ran the ordinary course. This was followed within a few weeks by an attack of so-called rheumatism, which confined her to her bed for several weeks. At that time she had high temperature. The joints of the hands were chiefly affected. This attack of septic arthritis ten or eleven years ago left considerable deformity in the hands, which has persisted to the present time. She has been fairly free from pain in the hands until about two months ago.

In April, 1917, she had another attack of tonsillitis. Immediately following this in April and ever since the pain and swelling in all the joints of her fingers have been severe. The wrist-joints are also swollen and painful, and she has more or less pain in other joints of the body, as in the cervical and dorsal regions of the spine. On account of the pain and swelling in the hand she has been unable to write in the usual way.

As you see (Fig 79), the hands present the picture of the condition described as arthritis deformans. The joints are greatly swollen and she is not able to use them as previously. The pain is also quite severe. The radiograph of these hands, however, shows no bony changes. The heart action has been rapid (about 100 to 110), although examination reveals no organic lesion. The examination of the urine shows it to be normal

with, perhaps, the exception of a slight amount of indican; slight traces of indican, however, are so often present in the urine of active normal individuals that this can scarcely be considered abnormal. The blood examination is also practically negative.

At the present time all such conditions are known to be due to a focus of infection somewhere in the body, and it must be located and eradicated if these patients are to be helped.

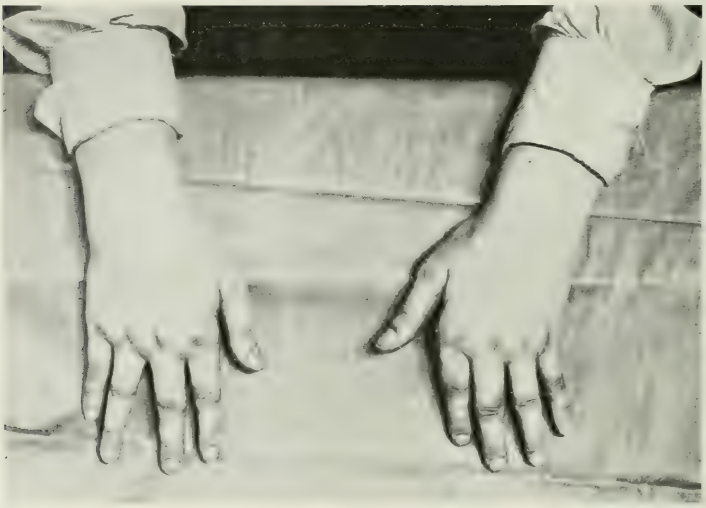


Fig. 79.—Photograph of hands of patient suffering with multiple arthritis due to Gram-negative diplococcus infection of tonsils. This photograph was taken when she first came for treatment.

In our search for such foci of infection the tonsils are first to come under suspicion. We believe that about 26 per cent. of all cases of septic arthritis have their inception in a focus of infection located in the crypts of the tonsils. Abscesses around the apices of the teeth are responsible for about 18 to 20 per cent. of the conditions. Next in order are infections of the nasal accessory sinuses and the ears. Absorption of toxins from the gastro-intestinal tract is likewise responsible for a certain percentage of these conditions.

Examination.—Her nasal and accessory sinuses and ears

reveal no foci of infection. Her sinuses are perfectly clear on transillumination and there is no purulent discharge from the ears or nose. Examination of the tonsils is more productive of results. The proper examination of the tonsils is important; it is accomplished first by inspection of the tonsils, their crypts and the tissue surrounding them, especially the anterior pillars. The crypts must be examined bacteriologically. The tonsils should also be investigated with a probe, to see if there is a foul odor within the crypts, and by pressure, which will reveal free pus if present.

Upon investigation we have found this patient's tonsils to be moderate in size, of the submerged type, and with numerous crypts. This type, while small in size, is perhaps productive of more harm to the system than the large tonsil with good drainage, which produces disturbance chiefly by its size. You will notice also that the anterior pillars of her tonsils are congested and reddened, a sign of considerable importance in these patients. By plunging a small cotton-wound applicator into some of the crypts we obtain a very foul odor.

We now pass from the physical examination of the tonsils to the more important and exact method of bacteriologic examination. This has been accomplished by passing a sterile curved platinum loop in the crypt of the tonsil whose oral surface has been swabbed with 95 per cent. alcohol. The loop is smeared across a plate containing blood-serum or glycerin-agar. The culture from her tonsils showed a Gram-negative diplococcus. Unless great care is exercised in obtaining such cultures much contamination will result on the plate after twelve or twenty-four hours' growth.

We have found, therefore, infection in the crypts of the tonsils by a Gram-negative diplococcus. Absorption of toxins from this organism is the probable cause of her infectious arthritis.

We shall next investigate the condition of her teeth. This is most satisfactorily carried out by having a radiograph made and careful inspection by a competent dentist in conjunction with the radiograph. Infections are frequently found both in the

teeth and tonsils. The radiograph of her teeth shows some root canals not filled and a possible area of absorption from one of the roots of the second upper molar on the right side. There seems to be shown in this film a slight absorption of the end of one of the roots itself. The radiographic findings in teeth are not always absolute, but they are highly suggestive, and the actual conditions found upon extraction are usually somewhat worse than is revealed by the *x*-ray film.

Upon inquiry as to her intestinal condition, she reports that the bowels move every day without the use of laxatives. As there is only a trace of indican in her urine it seems there is no intestinal stasis.

It is apparent, therefore, that the infectious arthritis is most likely due to the absorption of toxins from the tonsils and possibly also some from her right upper second molar.

We have made numerous blood-cultures from these patients in whom this organism was believed to be the cause of the systemic condition, and everyone has been negative. We have, however, had a report from Dr. Cotton, of the Trenton State Hospital for the Insane, of one fatal case in which he found a Gram-negative diplococcus in the spinal fluid; he also found this organism in a tooth abscess in that patient.

Prognosis.—The prognosis in cases of infectious arthritis is doubtful. We have seen many of them clear up after the removal of the primary focus of infection, but, on the other hand, have seen a considerable number which were either not much improved or actually became progressive.

Dr. Virgil P. Gibney recently wisely said that the cure of an arthritis is not always phenomenal after the removal of a focus of infection. Recovery does not take place in a short time. Dr. Gibney said this particularly about osteo-arthritis, but it also applies to such conditions as you have before you.

Treatment.—The modern treatment of infective arthritis consists in locating the focus of the infection and eradicating it. The most satisfactory plan is to inject autogenous vaccines until the activity of the infection has ceased and then remove the tonsils by complete enucleation. Carrying out such a plan,

an autogenous vaccine has been prepared from the crypts of this patient's tonsils. She has now had five injections of the vaccines and her condition is improving. She has also been advised to have the upper second molar on the right side extraced. Her general appearance is improved and she says she feels much better. She can now do more with her hands and she can write with more ease than for some time (Fig. 80). As you can see from the chart (Fig. 81), the temperature, which has been just above normal, is gradually coming down to the normal line and

Fig. 80.—Photograph of hands taken one month later, showing marked improvement.

her pulse-rate has been reduced from about 100–110 to 74–80. The mere fact that her pulse-rate has been reduced to about normal shows the marked benefit to the heart by cutting off the source of the systemic infection. This reduction in the pulse-rate has been noticed in a number of our cases similarly treated by autogenous vaccines. When the activity of her infection has ceased we will then enucleate her tonsils, after which, in the course of time, we believe the joints will approach a normal appearance and function.

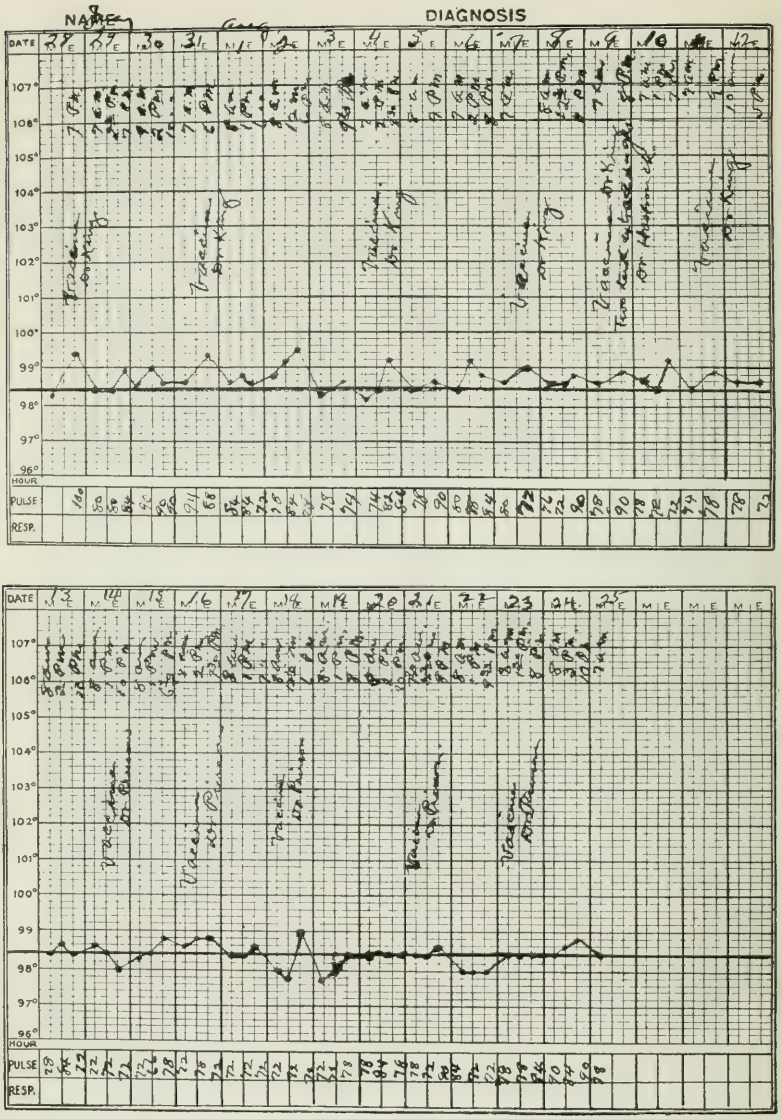


Fig. 81.—Case II.

The autogenous vaccines are prepared for each individual patient with considerable care. The culture is made from the crypts of the tonsils. An abscess which drains freely will cause

little systemic effect; the bacteria in the crypts of the tonsils cause the systemic effect. By swabbing the throat with 95 per cent. alcohol, and carefully securing the culture from the crypts, we are more likely to procure an efficient vaccine. We have made observations of individual vaccines in a large number of patients and certain facts have been impressed upon us. If the original cultures are many times transplanted, the potency of the resulting vaccines is lessened. We have found it desirable to make a vaccine from a young culture. The potency of vaccines from cultures of different ages varies materially with the different organisms. Some organisms will not yield a potent vaccine unless the vaccine is made from a culture of twelve to sixteen hours' growth. The Gram-negative diplococcus in this patient seems to yield the most potent vaccine when made from a culture of twenty-four to thirty-six hours' growth. If the vaccine is made from a culture much older the efficiency, in our observation, has been almost nil.

The vaccines are prepared so that 1 c.c. represents 200,000,000 of the organisms. The dosage for the average adult is 1 c.c. three times a week. We usually begin with a dose somewhat under 200,000,000 and gradually increase it to 200,000,000, or slightly more, providing the reaction is not great. There is generally a local reaction at the site of the injection manifested by various degrees of pain, swelling, and redness. The injections are given at points where there is sufficient subcutaneous tissue, either in the arms or buttocks. The arm just above the elbow is a convenient location for the injection. Some of our patients have been so emaciated that it has been difficult to find a suitable place for the insertion of the needle. Very thin patients, as a rule, complain more of the reactions than do the well nourished.

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